## Inventory of Projects

## Progress Report: Implementation of
## A Public Health Action Plan To Combat Antimicrobial Resistance (Part I: Domestic Issues)

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Focus Area I: Surveillance** | | | |
| **Action Item #1: Determine Which Organisms and Susceptibility to Specific Antimicrobial Drugs Should Be under Surveillance and Create a Mechanism for Periodic Updating of This List.** | | | |
| CDC, USDA, FDA, DoD, VA | Public Health Surveillance | Organisms currently under public health surveillance for antimicrobial resistance include: Campylobacter, *E. coli* O157:H7, Gram negative and Gram positive organisms causing health care associated infections, group A Streptococcus, group B Streptococcus, *Haemophilis influenzae* , *Helicobacter pylori* , HIV, Influenza, Malaria, *Mycobacterium tuberculosis* , *Neisseria gonorrhoeae* , *Neisseria meningitidis* , *Pneumocystis carinii* , Salmonella, Shigella, *Staphylococcus aureus* , *Streptococcus pneumoniae* , *Streptococcus pyogenes* , and *Trichomonas vaginalis* . Organisms are added to this list when resistance emerges as a public health problem, as tools are developed for detecting resistance, and when there is capacity at the appropriate level. | Ongoing. |
| ****TOP PRIORITY****<br>**Action Item #2: With Partners, Design and Implement a National AR Surveillance Plan.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC, FDA, NIH, USDA | Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria | NARMS is a collaboration among CDC, FDA (Center for Veterinary Medicine) and U.S. Department of Agriculture (Food Safety and Inspection Service and Agricultural Research Services). Fifty state and four local public health department laboratories forward every 20th non-Typhi Salmonella, Shigella, and *E. coli* O157 , and every Salmonella typhi, to the CDC NARMS laboratory for antimicrobial susceptibility testing. Additionally, ten states, who also participate in FoodNet, submit the first Campylobacter isolate received each week to the CDC NARMS laboratory. In 2001, NARMS launched the "Retail Food Study." Currently, nine participating states test various products for enteric bacteria. Through NARMS, CDC provided support to the Michigan Department of Health for a program on appropriate use of antimicrobial agents in agriculture. This will foster collaboration between the state public health department and state agriculture (veterinary diagnostic) laboratories. CDC is helping to develop a community-based program on appropriate use of antimicrobial drugs in animals. | Ongoing. NARMS has been expanded to all 50 states, providing national surveillance for antimicrobial resistance among foodborne pathogens. A third arm of NARMS testing retail meat samples has been added. The third testing site is FDA's Center for Veterinary Medicine's Office of Research. Foodnet sites submit Salmonella, Campylobacter, Enterococci, and *E. coli* isolates isolated from retail meat and poultry samples to the FDA -CVM Office of Research laboratory, where they are tested for susceptibility to a panel of antimicrobial agents. |
| CDC, DoD | Gonococcal Isolate Surveillance Project (GISP) | Sentinel surveillance system for monitoring AR of Neisseria gonorrhoeae in the United States established in 1986. Male urethral gonococcal isolates together with clinical and demographic patient data are submitted for susceptibility testing each month from STD clinics in approximately twenty-seven cities in the United States. GISP data demonstrate the ongoing spread of fluoroquinolone-resistance and the emergence of N. gonorrhoeae with decreased susceptibility to azithromycin in the U.S. GISP data are published in an annual report and periodically in the MMWR. (http://www.cdc.gov/std/gisp) contains GISP annual reports from 1998-2002 as well as important reference and link resources. | Ongoing. GISP data were used to revise the latest version of CDC's Sexually Transmitted Diseases Treatment Guidelines which were published in 2003. Data from 2003 will be available by Fall 2004. |
| CDC, FDA | Surveillance Planning | Coordinate surveillance activities. Initial meeting was held with CDC April 2001. Interagency cooperation remains a high priority within the department. Information sharing and coordinated activities continue to increase between agencies. | Ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Enhanced collection and electronic transfer of data on Antimicrobial Use and Resistance (AUR) | A cooperative study of enhanced collection, compilation, and transmission of data on antimicrobial use and resistance from automated laboratory instrumentation systems in healthcare settings to CDC and other public health systems using architecture fully compatible with NEDSS. This will create a database that will facilitate benchmarking and performance feedback to promote local AR improvement efforts; development of regional, state, and national data about patterns of use and resistance; and evaluation of prevention programs. | Ongoing. During 2003, TheraDoc software was modified to successfully create HL7 Version 3 messages containing microbiology susceptibility data from a pilot healthcare facility. This data complies with the AUR module of the National Healthcare Safety Network (NHSN) which will replace the National Nosocomial Infections Surveillance (NNIS) System. During 2004, TheraDoc software will be modified to create HL7 Version 3 messages containing pharmacy and Admission/Discharge/Transfer (ADT) data from the pilot facility. |
| CDC | Including AR surveillance in electronic laboratory-based reporting activities in the NEDSS | Develop, demonstrate, and implement automated, electronic reporting of susceptibility findings to health departments by using nationally-recognized data transmission and coding standards and sending the data through CDC's secure data network. The result of this project will enable various other AR surveillance activities to be used for this electronic communications medium. During 2002, beta-testing of a NEDSS based system with unique program area modules (PAM) began. | Ongoing. NEDSS continues to expand its capacity to report laboratory-based susceptibility findings. |
| CDC | Active Bacterial Core Surveillance (ABCs) | At Emerging Infections Program sites (EIPs), surveillance is conducted for invasive bacterial diseases due to pathogens of public health importance. For each case of invasive disease in the study population, a case report with basic demographic information is filed and, in most cases, bacterial isolates from a normally sterile site from patients are sent to CDC for laboratory study. System tracks emerging AR in isolates of *Streptococcus pneumoniae* , group A and group B streptococcus, and *Neisseria meningitidis* . Data provide an infrastructure for further research, such as special studies aimed at identifying risk factors for disease, post licensure evaluation of vaccine efficacy, and monitoring effectiveness of prevention policies. Program remains one of the most accurate and comprehensive surveillance tools available | Ongoing. ABCs produces yearly summaries on emerging resistance within the 10 EIPs (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee). An eleventh site, Texas, was added in 2004. |
| CDC | Translating lessons learned from ABCs to guide surveillance for drug-resistant *Streptococcus pneumoniae* (DRSP) in local and state health departments | A series of activities aimed at translating the lessons learned from ABCs for implementation in local and state health departments where information on DRSP is needed, but resources are limited and the goals of surveillance are more local in scope. A DRSP surveillance coordinator will work with the Get Smart team to support surveillance associated with the state-based appropriate antibiotic use projects as well as surveillance programs in other states. | Ongoing. A surveillance coordinator was hired in March 2004. The coordinator is assisting in the development, implementation, and support of state-based AR surveillance programs, as well as facilitating communication and interaction between sites. The online DRSP surveillance manual is being completed. Planning for the 2005 AR surveillance conference is ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | The National Nosocomial Infections Surveillance (NNIS) System. | A cooperative effort between the CDC and >300 hospitals to create a national nosocomial infections database. The database is used to reveal the epidemiology of nosocomial infections and to show AR trends, among other purposes. | Ongoing. The data from the NNIS System are reported annually in the NNIS Report which appears on the NNIS Web page (http://www.cdc.gov/ncidod/hip/SURVEILL/NNIS.HTM) and in the December issue of the American Journal of Infection Control. |
| CDC | Surveillance projects of HIV antiretroviral drug resistance | Surveillance for HIV antiretroviral drug resistance among different populations (adult, adolescent, and pediatric) and geographic areas in the U.S. using different methodologies, focusing on genotypic testing but also including phenotypic testing. Determine transmission of drug-resistant strains to previously uninfected persons and from mother to infant. Results support experts in deliberating potential recommendations for antiretroviral resistance testing before treating drug-naïve new patients. Results also provide information to guide regimens for post-exposure prophylaxis and prevention of mother to child transmission during pregnancy and delivery transmission. Could contribute to evaluation of success of risk prevention measures directed towards HIV-seropositive patients in treatment. | Ongoing. Funds awarded to participating state and local health departments. Laboratory characterization of transmitted HIV identified in drug-naïve persons was continued and data analyzed. The data highlighted the clinical implications of various key mutations. Novel methods for rapid phenotypic detection of drug resistance were published:1) Garcia-Lerma et al. (2002) Antimicrobial Chemotheraphy, 50:771-774.2) Qari et al. (2002) Antiviral Therapy, 7:131-139. In 2003, began antiretroviral resistance testing among newly diagnosed persons with HIV in the Pilot Antiretroviral Drug Resistance Testing (ARVDRT) Project in four project areas. In addition to these four pilot areas, 17 state, local, and territorial health departments will begin antiretroviral resistance testing among newly diagnosed persons with HIV in 2004, with more areas being added in subsequent years. |
| CDC | National Tuberculosis Surveillance System (NTSS) | Ongoing collection, analysis, and communication of national tuberculosis surveillance information; expanded in 1993 to include the frequency and type of AR, enabling strategically focused tuberculosis control and elimination efforts. The expanded national TB surveillance system has proven its usefulness in assisting in the evaluation of the success of TB control efforts and monitoring the status of the epidemic, particularly through the collection of data on initial drug susceptibility. Information on the use of initial regimens of four first-line drugs, directly observed therapy, and completion of therapy in one year or less have been used as measures to evaluate program success. As future efforts towards TB elimination increase, both existing and new surveillance systems at the national, state, and local levels will become even more critical to monitor the burden and impact of TB, evaluate the success of control and prevention efforts, and direct planning and policy development. | Ongoing. Data collection and analysis are gathered on a continuous basis. Since 1993, when the case report was expanded to include drug susceptibility results, the proportion of patients with primary MDR TB decreased from 2.5% to 1.0% each year during 1998-2001, with an increase to 1.2% in 2002. In 2002, the percentage of U.S.-born persons with MDR TB increased, from 0.6% in 2001 to 0.8% in 2002. However, of the total number of reported MDR TB cases, the proportion occurring in foreign-born persons increased from 31% in 1993 to 72% in 2002. Tables 8, 9, and 32 of the CDC annual TB surveillance report, Reported Tuberculosis in the United States, 2002, provide detailed summaries of anti-TB drug resistance from the national surveillance data. This report and other publications and recommendations based on these data are available on the internet (http://www.cdc.gov/nchstp/tb/default.htm). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Estimate of the burden of MRSA disease in hospitalized adults | This project uses existing datasets to measure the annual incidence of MRSA disease in hospitalized adults. | In 1999-2000, there were 292,687 hospitalizations with diagnosis of *S. aureus* infection estimated annually, accounting for 0.8% of hospital discharges. The average methicillin resistance rate was 42.0%. 119,760 hospitalizations with diagnosis of MRSA infection were estimated annually, including 30,015 septicemias, 26,726 pneumonias, and 63,019 other infections, accounting for 0.3% of hospital discharges. Estimates in non-hospitalized persons are planned for 2003. Manuscript submitted. |
| CDC | The epidemiology of MRSA strains in the U.S., using PulseNet | PulseNet is an innovative, laboratory-based national surveillance program that tracks the pulse-field gel electrophoresis (PFGE) profiles of selected bacteria. In collaboration with state health departments, MRSA strain types and their AR profiles in the U.S. are monitored through PulseNet to determine similarity with MRSA strains throughout the country, the prevalence of MRSA strain types from which vancomycin-intermediate strains of MRSA are derived, and similarity of U.S. epidemic strains of MRSA to those known to cause outbreaks and epidemics in Europe, Canada, and the Far East. | Ongoing. Data from this nationwide system have already been used to begin to understand the spread of specific MRSA strains among certain groups of patients in hospitals and in the community and will provide a clearer picture of the pathogenicity of *S. aureus* and the spread of AR among staphylococci. Recent PFGE data have been extremely useful for monitoring the spread of MRSA isolates in the United States. PFGE data have indicated the presence of seven major clonal lineages or pulsed-field types (PFTs) of MRSA in the U.S. Four PFTs are common among healthcare related strains, two PFTs are found primarily among community-acquired isolates, and one is found among strains from both healthcare and community-acquired strains. In 2003, two additional MRSA types, community among community MRSA strains have been identified. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Surveillance for Emerging Antimicrobial Resistance Connected to Healthcare (SEARCH) | Normally, vancomycin is the most reliable and effective drug for treating MRSA. The appearance of MRSA with reduced susceptibility [to vancomycin] (vancomycin-intermediate *Staphylococcus aureus* [VISA]), and resistance (vancomycin-resistant *Staphylococcus aureus* [VRSA]) is concerning and may be a warning that strains resistant to vancomycin could soon appear. SEARCH is a network of voluntary participants (i.e., hospitals, private industries, professional organizations, and state health departments) which have joined together to report the isolation of *Staphylococcus aureus* with reduced susceptibility to vancomycin. All U.S. healthcare organizations or practitioners are encouraged to report such isolates to SEARCH and, after notifying their state health department, to send the isolates to CDC for confirmatory testing. SEARCH enhances the ability to detect these pathogens, which have a high public health importance but are difficult to detect through traditional surveillance systems, and provides confirmatory diagnostic and expedited susceptibility testing for these isolates | Ongoing. To date, CDC has identified eight VISAs and three VRSAs in the U.S. Updated guidance on appropriate testing was sent to State Health Departments in April, 2003. |
| CDC | MRSA carriage in rural Alaska | In recent years, several community outbreaks of MRSA skin infections have occurred among Alaska Natives. This is a survey of the frequency of MRSA nasal colonization in twelve rural Alaska communities. The findings will be disseminated to affected communities and health care providers to help promote appropriate antimicrobial drug use and promote prevention of MRSA skin infections. | Ongoing.<br>Baggett HC et al. Community-onset methicillin-resistant *Staphylococcus aureus* associated with antibiotic use and the cytotoxin Panton-Valentine leukocidin during a furunculosis outbreak in rural Alaska. Journal of Infectious Diseases. 189(9):1565-73;2004<br><br>Baggett HC et al. An outbreak of community-onset methicillin-resistant *Staphylococcus aureus* skin infections in southwestern Alaska. Infection Control & Hospital Epidemiology. 24(6):397-402;2003 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Antimicrobial resistant early-onset sepsis and maternal intrapartum antibiotic use | Increased use of antibiotic prophylaxis during labor and delivery to prevent perinatal group B streptococcal (GBS) disease has decreased the rate of early-onset GBS infections by 70%. As more antimicrobial drugs are used in the labor and delivery setting to prevent mother-to-child transmission of group B streptococcus, the risk of newborns acquiring infections with other perinatal pathogens, such as *E. coli* drug resistant infections might increase. The objectives of this project were to monitor trends in early-onset infections with non-GBS pathogens including drug resistant *E. coli* in selected areas, to evaluate whether antimicrobial drug use during labor and delivery was associated with an increased risk of drug resistant E. coli, and to assess the impact of a penicillin G shortage on prophylactic use of penicillin, ampicillin, and other agents during labor and delivery. | Surveillance for non-GBS sepsis is ongoing in the Active Bacterial Core Surveillance (ABCs) with a new surveillance area, MN, starting case finding in 2004 . To date surveillance has led to two publications summarizing data from CT , GA, and CA ; recent data were presented at the International Conference on Emerging Infectious Diseases, 2004. Evidence that the rate of resistant *E. coli* infections increased among preterm infants, particularly among very low birthweight infants from 1998-2000, raised concern. A recent analysis of incidence trends, however, found a 30% decline in non-GBS sepsis due to all causes from 1998-2002 and stable rates of *E. coli* sepsis and ampicillin-resistant *E. coli* sepsis. Moreover, among preterm infants, the proportion of *E. coli* isolates that were ampicillin resistant did not increase significantly. Additionally, a review of a random sample of births in 2003 and 2004 is planned for these surveillance areas to evaluate antibiotic agents used for GBS prophylaxis, with a particular focus on use of vancomycin and on the impact of a new penicillin G shorta |
| CDC | The *Helicobacter pylori* Antibiotic Resistance Program (HARP) and Antimicrobial resistance in Helicobacter pylori in Alaska | HARP conducts prospective, long-term monitoring of trends in AR to guide treatment regimens for *H. pylori* infections. Twelve academic medical centers throughout the United States submit *H. pylori* isolates and clinical and epidemiologic data from endoscopically-diagnosed patients monthly. Resistance is tested at CDC. Resistance and epidemiologic data are entered into a database at CDC for analysis of prevalence, risk factors and regional trends in rates of antimicrobial resistance in *H. pylori* strains. The monitoring laboratory is also used for ongoing collaborative CDC-Emory-Veterans' Administration Medical Center research of *H. pylori* and peptic ulcer disease, and is a future platform for collaborative studies between academia, public agencies, and industry. A sentinel surveillance system for *H. pylori* has been established in Alaska to monitor antimicrobial resistance among Alaska Natives who have high rates of *H. pylori* infection; and where AR among *H. pylori* is high. A study of the rates of reinfection with *H pylori* after treatment is being conducted in urban and ru | Ongoing. Susceptibility testing methods established by FDA and National Committee on Clinical Laboratory Studies (NCCLS) for antimicrobial susceptibility testing of *H. pylori* were validated, and the minimum inhibitory concentration with quality control limits for antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, and tetracycline have been determined. Analysis of data from HARP show that nearly 40% of isolates are resistant to one or more first-line antimicrobial agents. These findings may form the basis of recommendations for treatment. Sentinel surveillance for H pylori in Alaska continues.Completion of the urban Alaska Native arm of *H. pylori* reinfection study in Alaska was completed and recruitment for the other arms is in progress. Reinfection with *H. pylori* after successful treatment was observed 14.5% of persons during the 2 years of follow-up. Clarithromycin resistance among *H. pylori* was associated with past antimicrobial use of macrolides and led to higher rates of treatment failure using clarithromycin-based regimens. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Molecular tools for the control and epidemiology of head and body lice | Evaluate new molecular tools for monitoring louse populations and determining the role of insecticide resistance in louse infestations and re-infestations to design and implement appropriate control strategies. Characterize local populations of lice and the global relationships and movements of louse populations. Ascertain the genetic relationships of head, body, and pubic lice. When completed, the data generated will improve knowledge of the epidemiology of insecticide resistance in louse populations and improve prevention and control strategies. | Ongoing. In 2001, collected head and body lice from over ten states and seven countries, and sequenced over 700 clones from gene libraries. In 2002, the microsatellite markers developed through sequencing of head and body louse libraries were applied in field studies of head and body louse population biology and micro-epidemiology of insecticide resistance. In 2003, use of microsatellites developed at CDC were used in field studies in Nepal and Mongolia by collaborators at the University of Queensland, Australia to provide convincing evidence that head and body louse populations were, in fact, separate species. Moreover, pyrethroid resistance gene mutations were found in head louse samples submitted by our collaborators in Denmark and California. These studies are providing the data needed to assess the interaction of multiple resistance alleles and louse micro-epidemiology around the world, and will result in rapid increase in our understanding of louse resistance and micro-epidemiology. |
| CDC | Testing of drug-resistant *Trichomonas vaginalis* | Trichomoniasis is the most common curable STD in young, sexually active women. This project includes passive surveillance for *Trichomonas vaginalis* resistance among isolates from patients whose infection has not resolved after at least two courses of standard metronidazole therapy. Parasites are tested both aerobically and anaerobically for sensitivity to metronidazole and to tinidazole, which, outside the United States, is the most common alternative therapy for trichomoniasis. These data will identify molecular markers of metronidazole-resistant strains, allow investigation of drug-resistance mechanisms, and will be utilized to identify alternative chemotherapeutic agents. | Ongoing. Testing is an ongoing service of CDC. In 2001, initiated testing on isolates obtained through the Grady Adolescent STD Project (GRASP) to determine the prevalence of metronidazole-resistant *T. vaginalis* isolates in an urban adolescent clinic. Isolate testing and data analysis is an ongoing process and results will prove useful in identifying alternate therapies. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Enhanced surveillance of influenza viruses for resistance to licensed drugs and development of tests for rapid detection of drug-resistant strains with pandemic potential | Improved molecular tests for rapid diagnosis of mutants resistant to both the old and new drugs are needed for pandemic preparedness as well as for interpandemic control of influenza. This project studies avian influenza viruses of different subtypes, which will improve pandemic preparedness. In addition, it will evaluate existing biochemical tests and develop new molecular techniques for detecting influenza A and B mutants resistant to neuraminidase inhibitors (NIs), which will improve surveillance for drug-resistant variants among human influenza viruses. | In 2001, compared assays for resistance of influenza viruses to NIs to determine the most adequate method for further use in detecting of NI-resistant strains, and analyzed sequencing data available for avian influenza viruses. In 2002, two neuraminidase (NA) assays, fluorescence (FL) and chemiluminescent (CL), were applied to routinely monitor more than a thousand influenza field isolates collected worldwide. In 2003, the use of the CL neuraminidase assay for routine surveillance of human influenza viruses circulating worldwide was continued. Antigenic and genetic analysis of viruses with different susceptibility to NIs was performed. Molecular and biological techniques previously developed at the Influenza Branch were used for monitoring the sensitivity of avian influenza viruses with pandemic potential to licensed NIs. It was shown, in particular, that two influenza A(H5N1) viruses isolated from humans in Hong Kong in February of 2003 were resistant to adamantanes. The sensitivity of these two isolates to NIs was demonstrated. |
| DoD | Development of a DoD AR surveillance plan consistent with the national AR surveillance plan | Establish an overarching framework for facilitating the implementation, operation, and evaluation of activities in AR surveillance within DoD. | Ongoing. Leaders in infectious disease, laboratory, and preventive medicine in the three services are working to develop a common plan for AR surveillance in the DoD. |
| DoD | DoD antimicrobial resistance surveillance network | Under a Cooperative Research and Development Agreement (CRADA) with private industry, developing a DoD-wide AR surveillance network for identifying AR occurrences and trends within the military population. The cornerstones of this mechanism are: 1) the provision of daily, independent quality-assurance review and feedback of a military laboratory's susceptibility test results by experts in the field, 2) the continuous generation of up-to-date antibiograms based on an individual medical facility's AR patterns, 3) access to validated information on antimicrobial resistance occurrences and trends in the facility's geographic region for evaluating their implications for military personnel, and 4) facilitation of DoD-wide monitoring of AR trends to improve evidence-based decision and policy making on antibiotic usage and patient care, and 5) to enhance DoD ability to identify and respond to AR events of military significance in a timely manner. | Ongoing. Electronic antimicrobial susceptibility testing quality assurance and analysis system is being used in three pilot sites. Expansion to additional sites prepared and ongoing. Linkage of system into a DoD network for information sharing and analysis of AR trends initiated. Expansion of network and its evaluation planned for the next 2 to 3 years. |
| FDA | Proposed Rule – Surveillance/Reporting | Publish proposed rule regarding surveillance and annual reporting (included with proposed rule "Safety Reporting for Human Drug and Biologic Products"). | Assessing economic impact of the proposed regulation. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Guidance - Surveillance Planning | Develop guidance relating to surveillance and annual reporting (based upon proposed rule "Safety Reporting for Human Drug and Biologic Products"). | Assessing economic impact of the proposed regulation. |
| VA | Emerging Pathogens Initiative (EPI) | The Veterans Health Administration (VHA) currently has an ongoing and well-defined AR surveillance plan (the EPI, a laboratory-based automated surveillance system). | Currently over 170 VHA facilities across the country transmit data to the EPI monthly. The data collected by the EPI are reviewed quarterly by the Infectious Diseases Program Office and reported to the Veterans Integrated Service Networks. Enhancements that will acquire additional information on antimicrobial resistance of specified organisms are anticipated to be distributed to reporting stations by July 1, 2004. |
| VA | Emerging Pathogens Initiative (EPI) | The VHA uses standardized definitions and methods to set local parameters for surveillance in the EPI system. Currently EPI data regarding some AR organisms are returned to the Veterans Integrated Service Networks quarterly with reporting station specific data included. National quartiles are also provided for use at the Network and local level. Confidentiality is a key element in any activity undertaken by the VHA. Great effort has been put forth to maintain confidentiality of the Emerging Pathogens Initiative surveillance data set. Access is strictly limited for any data with unique identifiers. | Ongoing. |
| **Action Item #3: Develop Standards and Methodologies.** | | | |
| CDC | Grant Program for Applied Research on Antimicrobial Resistance: Characterization of Strains of Community-Associated Methicillin-Resistant *Staphylococcus aureus* | This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus* (*S. aureus*) causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques. | Five three years awards were made in 2003. Recipients are Harbor-University of California Los Angeles Research & Education Institute, University of California – San Francisco, University of Chicago, and William Beaumont Hospital. " |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Grant Program: Applied Research on AR - Validation of National Committee for Clinical Laboratory Standards (NCCLS) Breakpoints for Bacterial Human Pathogens | The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of NCCLS breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development. | Ongoing. Funded three programs in the Fall of 2002: University of Texas Medical Center, (Development of Interpretive Breakpoint Criteria for Neisseria Meningitidis); University of Pittsburgh, (NCCLS Interpretive Criteria for Salmonella); University of Wisconsin Medical Center, (Validation of NCCLS Methods and Breakpoints for Extended Spectrum beta-lactamases). Projects underway, results pending. |
| FDA | Development of NCCLS testing standards | Campylobacter is one of the primary foodborne pathogens under surveillance in NARMS, however, neither NCCLS standardized testing methods nor validated susceptible or resistant breakpoints exist. | Developed quality control ranges for the agar dilution method of testing Campylobacter. QC ranges have been incorporated into the current NCCLS performance standards. |
| USDA | QC testing as a part of NARMS | Methodologies and standards are being developed for testing of food safety pathogens as a part of NARMS. | Ongoing |
| **Action Item #4: Address Additional Surveillance Issues Unique to AR.** | | | |
| CDC | Specialized surveillance projects and treatment trials for drug-resistant tuberculosis | Information on the initial drug regimen prescribed, coupled with information on initial drug susceptibility results, allows a judgment about the adequacy of therapy and corrective action on individual cases of tuberculosis by public health officials and health care providers, if the regimen is judged to be inadequate or suboptimal. To improve knowledge of drug resistance in tuberculosis and effectiveness of alternate treatment regiments, CDC is conducting projects on the frequency of low-level INH resistance and resistant to quinolones, treatment of HIV-related tuberculosis using a rifabutin-based regimen, and a trial to determine the effectiveness of a new regimen for isoniazid-resistant tuberculosis. Results of these studies will describe prevalence and incidence of understudied resistance in tuberculosis and inform recommendations for new treatment regimens. | Ongoing. Current surveillance data can be obtained at: http://www.cdc.gov/nchstp/tb/surv/surv2002/default.htm |
| CDC | See Action Item #5 (monitoring antimicrobial use in community and correlating usage with resistance patterns). | See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns). | See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns). |
| FDA | Antimicrobial surveillance plan | Development of a surveillance plan for antimicrobial drug resistance among clinical laboratory isolates. | Ongoing. A five year option contract was awarded to Focus Technologies in October 2002. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | See Action Item #2 (Proposed Rule - Surveillance/Reporting). | See Action Item #2 (Proposed Rule Surveillance/Reporting). | See Action Item #2 (Proposed Rule - Surveillance/Reporting). |
| FDA | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). |
| **** TOP PRIORITY ****<br>**Action Item #5: Develop and Implement Procedures for Monitoring Antimicrobial Use In Human Medicine, Agriculture, Veterinary Medicine, and Consumer Products.** | | | |
| CDC | AUR: component of the National Nosocomial Infections Surveillance (NNIS) | The AUR component of NNIS allows participating hospitals to collect data on select antimicrobial agents and cumulative susceptibility data on select organisms identified by the clinical microbiology laboratories, allowing the calculation of a national estimate of the prevalence of antimicrobial-resistant organisms in hospitals and the amounts of select antimicrobial agents used in these hospitals. These data allow select AR rates to be compared among hospitals and provide better understanding of the relative importance of antimicrobial drug use vs. other factors (i.e., cross-transmission, severity of illness) for development of antimicrobial-resistant infections by several key pathogens | Ongoing. In 2001, implemented the AUR component and received data from fifteen hospitals. In 2002 twenty hospitals participated. A pilot system to electronically capture susceptibility testing results to simplify reporting was developed. Participation in 2003 was stable. |
| CDC | Monitoring antimicrobial use in the community and correlating usage with resistance patterns | Analysis of antimicrobial use databases has proven to be complex, requiring sophisticated statistical methods to adjust for the design of certain usage survey samples and requiring substantial medical consultation time to link drug use with appropriate clinical diagnosis codes and potentially with databases regarding resistant infections. This project will develop a core analytic team that will track antimicrobial drug use in the community and correlate results of use with drug-resistance patterns (using drug-resistant *Streptococcus pneumoniae* as the marker community-acquired respiratory organism) and with community intervention efforts. The team will review availability and appropriateness of antimicrobial use databases and focus on establishing baseline trends in prescribing for upper respiratory infections using NAMCS, National Hospital Ambulatroy Medical Care Survey (NHAMCS), state Medicaid databases, Synergy, and other databases provided through partners (e.g., Blue Cross/Blue Shield; specific managed care organizations). | Ongoing. In 2001, analyzed and published trends in prescribing for respiratory conditions in the community during the 1990s by using NAMCS and NHAMCS, initiated development of standard programs and documentation for regular analyses of three national or regional databases for drug prescribing, and provided technical support to five intervention programs or partners. During 2002, completed and published analysis of national data on trends in antibiotic prescribing for children for upper respiratory infections (McCaig et al. JAMA June 2002), issued new recommendations for alternative antibiotics for group B streptococcal prophylaxis for penicillin allergic women. During 2003, published analysis of national data on trends in antibiotic prescribing in ambulatory care settings (McCaig et al. EID April 2003). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | National Ambulatory Medical Care Survey (NAMCS) and National Hospital Ambulatory Medical Care Survey (NHAMCS) | An annual national survey that collects data on the utilization of ambulatory medical care services provided by office-based physicians in the united States. Findings are based on a sample of visits to nonfederally employed office-based physicians who are primarily engaged in direct patient care. NAMCS monitors trends in prescription of antimicrobial drugs in the physician office setting.<br>NHAMCS is an annual national survey that collects data on the utilization of ambulatory medical care services provided by hospital emergency and outpatient departments in the United States. Findings are based on a sample of visits to emergency departments and outpatient clinics. NHAMCS monitors trends in prescription of antimicrobial drugs in hospital emergency and outpatient departments. | Ongoing. During 2002, completed and published analysis of national data on trends in antibiotic prescribing for children for upper respiratory infections (McCaig et al. JAMA June 2002), issued new recommendations for alternative antibiotics for group B streptococcal prophylaxis for penicillin allergic women. During 2003, published analysis of national data on trends in antibiotic prescribing in ambulatory care settings (McCaig et al. EID April 2003). Recent NAMCS and NHAMCS methodology, data, and reports are available on the internet: (http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm" |
| CDC | Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* in healthcare facilities | This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System (TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies. | Ongoing. Initiated pilot testing of the interventions in two hospitals within the network (University of Pittsburgh Medical Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital) during 2001. Follow-up observations show significant improvement in compliance across all occupations. Problems hindering compliance which continue to be targeted include unreliable delivery of isolation materials, inconsistent identification of patients requiring isolation, and time consuming inefficiencies in the delivery of patient care services such as medication administration. In addition, an assessment of policy, perception, and practice regarding MRSA control has been initiated. In 2003 a survey of knowledge, attitudes, and practices in facilities was conducted and evaluated TPS in an inpatient surgical unit at PRHI which measured a decline of 54% in healthcare associated -MRSA infections. |
| DoD | Prescription databases | Use of the prescription database (PDTS) is being piloted for gastrointestinal and respiratory outbreak detections. | In 2001, DoD developed a prescription database as part of a patient safety program. This database is used principally to screen for drug-drug interactions resulting from patients filling their prescriptions in more than one medical treatment venue. A DoD syndromic surveillance system (ESSENCE) has piloted the use of this data as a potential early signal for disease outbreaks. When DoD AR surveillance is more mature, further use of the database can be attempted for detecting AR trends in association with prescription practices and disease occurrences." |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | See Action Item #4 (Antimicrobial surveillance plan) | Review private sector surveillance data to determine whether it has potential to support FDA/CDER regulatory and scientific activity. | See Action Item #4 (Antimicrobial surveillance plan) |
| FDA | See Action Item #2 (Proposed Rule Surveillance/Reporting). | See Action Item #2 (Proposed Rule Surveillance/Reporting). | See Action Item #2 (Proposed Rule Surveillance/Reporting). |
| FDA | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). |
| **Action Item #6: Identify and Evaluate Methods for Collecting (e.g., Optimal Sampling Methods) and Disseminating the Surveillance Data on Antimicrobial Drug Use.** | | | |
| FDA | See Action Item #4 (Antimicrobial surveillance plan) | See Action Item #4 (Antimicrobial surveillance plan) | See Action Item #4 (Antimicrobial surveillance plan) |
| FDA | See Action Item #2 (Proposed Rule Surveillance/Reporting). | See Action Item #2 (Proposed Rule Reporting/Reporting). | See Action Item #2 (Proposed Rule Reporting/Reporting). |
| FDA | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). | See Action Item #2 (Guidance). |
| VA | Emerging Pathogens Initiative (EPI) | Resistance data are being gathered in the EPI, an automated surveillance system, at the reporting site level and can be used for comparisons based on geographic areas and can be linked to ICD-9-CM diagnostic codes. In addition, drug use data can be linked to laboratory testing and diagnoses for a significant emerging disease. | This item is already underway in the VHA with reporting from facilities across the country. Enhancements that will acquire additional information on antimicrobial resistance of specified organisms are anticipated to be distributed to reporting stations by July 1, 2004. |
| **Action Item #7: Work With Accrediting Agencies To Address Antimicrobial Drug-Use As Part Of Quality Assurance In Health Care Delivery Systems.** | | | |
| CDC | Get Smart: Know When Antibiotics Work | CDC and the National Committee for Quality Assurance developed two new performance measures for the 2004 Health Plan Employer Data and Information Set (HEDIS®). HEDIS® is a performance measurement tool used by purchasers and consumers to compare many of the nation's leading health plans. The new measures assess the appropriate treatment of children with pharyngitis and with upper respiratory infections for the treatment acute bronchitis and all upper respiratory infections in adults. | HEDIS® 2004 is currently available online at: http://www.ncqa.org/Programs/HEDIS/HEDIS%202004%20Info.htm |
| **Action Item #8: Ensure That Clinical Laboratories That Provide Data for AR Surveillance Purposes Have Access to and Routinely Participate in Pertinent Training and Proficiency Testing Programs with Good Performance and Indicate AR Testing Methodologies in Their Surveillance Reports (e.g., Specific Automated Methods or Manual Techniques).** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Preventing Lab Errors: CD-ROM for susceptibility testing | New antimicrobial agents and new resistance patterns pose a challenge to clinical laboratories because testing methods vary with organism/antimicrobial agent combinations. NCCLS standards outline recommended procedures, but they are difficult for some laboratories to interpret. This CD shows laboratories how to apply NCCLS standards, demonstrates the modes of action of each group of antimicrobial agents and the mechanisms organisms develop to resist the agents, describes quality control procedures needed to verify accuracy of testing results, and demonstrates specific procedures laboratories must use to detect resistance in different organisms. | CD-ROM was completed in 2002 and has been distributed widely throughout the US and across the world. It is the backbone of the Washington State train-the-trainer workshops and has been give to over 1,000 participants in courses delivered by the NLTN on the subject of AST. An additional 15,000 have been mailed to laboratories by APHL. Available at : ast@aphl.org |
| CDC | Multilevel Antimicrobial Susceptibility Testing Educational Resource (M.A.S.T.E.R.) Program | The M.A.S.T.E.R. program, is a 3-phase project to upgrade the accuracy of antimicrobial susceptibility testing and reporting in the U.S. Currently, the Web site has case studies, a Q and A section, hot papers, and a list of references. | Ongoing. The website has received over 130,000 hits from 50 countries. Material from the website has been used in numerous training courses on susceptibility testing and is frequently cited as a resource in medical technology classes. The CD-ROM based training course; “Antimicrobial Susceptibility Testing: A Self Study Guide” received the CDC Communications Roundtable Award. Outstanding Electronic Media Program award in 2003. http://www.phppo.cdc.gov/dls/master/aboutmaster.asp |
| CDC | The National Laboratory Training Network (NLTN) | The National Laboratory Training Network (NLTN) delivers training around the country on proper methods of antimicrobial susceptibility testing and reporting. | The NLTN presented 48 courses for more than 12,000 participants between January 1, 2003 and April 30, 2004. The focus of these courses was the importance of using NCCLS standards for testing and insuring that reports given to clinicians provide correct information for appropriate treatment. Most of the courses are 5-6 hours long, but the NLTN also presented several nationwide teleconferences on related topics. The teleconferences account for about ½ of the participants. These courses are a major effort of the NLTN. The majority of courses are given as classroom presentations by the same speaker, in order to provide a consistent message to laboratories across the country. These will continue through July, 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | National Healthcare Safety Network (NHSN) | The NHSN will be an Internet-based nationwide network that will monitor trends in adverse events associated with invasive devices, procedures, and medications used in the delivery of healthcare. Under the NHSN's Medication-associated Adverse Event Module, initial focus will be on use and resistance of antimicrobial agents and on establishing electronic reporting of antimicrobial use and resistance data to increase efficiency, timeliness, and accuracy of the monitoring effort. When implemented, the NHSN will significantly enhance the ability to monitor and track trends of usage and resistance of microbes to antimicrobial agents in a variety of healthcare delivery settings. These data can then be used to enhance patient safety by enabling healthcare workers to develop and deploy strategies to prevent overuse and inappropriate use of these agents, as well as strategies to prevent other pathogens from becoming resistant. | Initiated. In 2001-2003, gathered requirements for system, held joint application development sessions with current and potential users, and started work on data model, security, standard nomenclature for pathogens and antimicrobial agents, and detailed use cases that define system functionality. In addition, work has been ongoing to develop the messaging specifications for electronic reporting from hospitals of antimicrobial use (from pharmacy systems) and resistance (from microbiology systems). In 2003, efforts to design, develop, and deploy the NHSN (deployment of version 1.0 scheduled for January 2005 ) were started. |
| CDC | AR research and reference testing | CDC reference laboratory conducts ongoing research and provides selected reference services for susceptibility testing of numerous bacterial species. | Ongoing. Recent achievements include the description of new AR mechanisms, which has led to modification and improvement of the testing methods used in clinical microbiology laboratories to detect resistance, evaluations of NCCLS methods completed and modifications made to improve accuracy, and evaluations of commercial susceptibility testing methods completed and problems noted to the manufacturers. Additional accomplishments include confirmation and investigation of phenotype and genotype of the first three vancomycin-resistant *Staphylococcus aureus* isolates in the United States. |
| CDC | *Mycobacterium tuberculosis* (Mtb) antimicrobial susceptibility testing program | Approximately 165 laboratories participate in this program designed to assess and enhance the ability of clinical laboratories to accurately test for AR. Most laboratories test for susceptibility to isoniazid, pyrazinamide, ethambutol and rifampicin, and streptomycin. Approximately 35 laboratories test nontuberculous mycobacteria in addition to susceptibility to other drugs. Laboratories can enter susceptibility test results through the online data entry system and view reports of results on a website address for each panel shipment for feedback. | Ongoing. |
| FDA | Pertinent training | Continue to ensure validity of antimicrobial susceptibility information derived from NARMS. | Developed both an antimicrobial susceptibility testing quality control and quality assurance program for the three arms of NARMS, human, slaughter plants, and retail meat. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #9: Evaluate the Performance of Licensed, Automated AR Testing Devices in the Context of Changing Resistance Patterns and Update Their Labeling When Appropriate (e.g., Changes in Quantitative Resistance That May Make a Test Result Invalid).** | | | |
| **Action Item #10: Working with Partners, Including National Committee for Clinical Laboratory Standards (NCCLS), Further Develop, Refine, and Promote Standardized Clinical, Epidemiologic, and Laboratory Methods for Documenting and Assessing the Significance of Drug Resistance Among Yeasts and Moulds, Parasites, and Viruses.** | | | |
| FDA | In-vitro antimicrobial susceptibility testing | Develop quality control standards for the in-vitro antimicrobial susceptibility testing of bacterial pathogens isolated from aquaculture foods. | Coordinated the development of a NCCLS guidance document (M42-R) for standardizing an antimicrobial disk susceptibility test method for bacteria isolated from aquatic species. Also, see item #4 (Campylobacter quality control development). |
| FDA | Devices containing antimicrobials guidance | Draft guidance document for industry: how the Center for Devices and Radiologic Health (CDRH) intends to regulate devices containing antimicrobial agents, and what information regarding efficacy and resistance CDRH wants to see in premarket applications (interim until rulemaking is completed). | In development. |
| FDA | HIV Drug Resistance Genotype Assay Guidance | Revised guidance on HIV Drug Resistance Genotype Assays. | Publication pending. |
| **Action Item #11: Identify Ways To Overcome Economic, Legal, and Other Barriers To Appropriate AR Testing and to the Reporting of Results (e.g. Sufficient Human Resources, Cost Considerations, Empiric Treatment Recommendations, Managed-Care Practices, etc.).** | | | |
| CDC | Economic modeling of diagnostic and treatment strategies for gonorrhea based on prevalence of AR | The increasingly widespread use of nonculture methods for gonorrhea diagnosis is a major challenge to monitoring AR in *N. gonorrhoeae* , especially in light of the emergence of ciprofloxacin-resistant gonococcal isolates from Hawaii (ciprofloxacin is first-line gonorrhea therapy). This project will examine which diagnostic and treatment strategies are more cost-effective when the proportion of *N. gonorrhoeae* that are ciprofloxacin-resistant is less than 5%: continue to use ciprofloxacin and implement more widespread susceptibility testing, or switch to a more expensive cephalosporin and not increase the scope of susceptibility testing. When completed, the results will help provide a rational basis for programmatic decisions both for selection of gonorrhea treatment and for use of laboratory resources. | Ongoing. |
| **Action Item #12: Pursue Legal Mechanisms for Manufacturers To Provide Otherwise Unavailable Drugs to Government Reference Laboratories for the Sole Purpose Of Antimicrobial Drug Susceptibility Testing (as part of surveillance) with the Understanding That These Drugs Will Not Be Used for Drug Discovery Purposes.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #13: With State Health and Agriculture Departments and Other Stakeholders, Define Needed Core Capacity (Human, Laboratory, and Electronic Resources) at the State and Local Level To Ensure That Basic AR Surveillance Is Conducted In These Jurisdictions. As Part of This Effort, Ensure That State Public Health and Veterinary Diagnostic Laboratories Maintain the Capacity To Test the Drug-Susceptibility Patterns of Resistant Organisms of Public Health Importance, Especially For Drug-Microorganism Combinations for Which Testing Mechanisms Are Not Routinely Available at Hospital and Commercial Laboratories.** | | | |
| **Action Item #14: Provide Resources To Assist In Meeting State and Local Core Capacity Needs for AR Surveillance. Strive To Provide Consistent Funding from Year to Year to State and Local Health and Veterinary Diagnostic Laboratories That Meet Quality Assurance Standards.** | | | |
| CDC | Support for state AR Surveillance | An AR coordinator will enhance communication and coordination between states and thus assist states meet capacity needs for improved AR surveillance. Resources provided will include: the online DRSP surveillance manual, intra-site communication tools, and site consultations, and the Get Smart campaign. The surveillance coordinator will provide technical assistance to funded sites and monitor surveillance activities on the state and local level. Specific surveillance techniques will be identified for each site according to available resources. | Ongoing. An AR surveillance conference is scheduled for 2005 and will allow collaboration between many AR stakeholders. Sections of the DRSP surveillance manual are available online now. The final version should be completed in 2004. |
| **Action Item #15: Provide an Accessible, Centralized Source of AR Data from Major Surveillance Systems Involving Animal and Human Populations. In Consultation with Stakeholders, Determine How To Report AR Data in a Way That Is Valid and Useful to Interested Parties (e.g., Clinicians, Public Health Officials, Veterinarians, and Researchers). Include Sufficient Detail in Surveillance Reports To Permit Local Analysis and Comparison with Trends in Drug Use and Medical and Agricultural Practices.** | | | |
| CDC, FDA, NIH, USDA | Expansion and enhancement of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria | NARMS is a collaboration among CDC, FDA (Center for Veterinary Medicine) and U.S. Department of Agriculture (Food Safety and Inspection Service and Agricultural Research Services). Fifty state and four local public health department laboratories forward every 20th non-Typhi Salmonella, Shigella, and *E. coli* O157 , and every *Salmonella Typhi* , to the CDC NARMS laboratory for antimicrobial susceptibility testing. Additionally, ten states, who also participate in FoodNet, submit the first Campylobacter isolate received each week to the CDC NARMS laboratory. In 2001, NARMS launched the “Retail Food Study.” Currently, nine participating states test various products for enteric bacteria. Through NARMS, CDC provided support to the Michigan Department of Health for a program on appropriate use of antimicrobial agents in agriculture. This will foster collaboration between the state public health department and state agriculture (veterinary diagnostic) laboratories. CDC is helping to develop a community-based program on appropriate use of antimicrobial drugs in animals. | Ongoing. NARMS has been expanded to all 50 states, providing national surveillance for antimicrobial resistance among foodborne pathogens. A third arm of NARMS testing retail meat samples has been added. The third testing site is FDA's Center for Veterinary Medicine's Office of Research. Foodnet sites submit Salmonella, Campylobacter, Enterococci, and E. coli isolates isolated from retail meat and poultry samples to the FDA -CVM Office of Research laboratory, where they are tested for susceptibility to a panel of antimicrobial agents. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC, DoD | Gonococcal Isolate Surveillance Project (GISP) | Sentinel surveillance system for monitoring AR of *Neisseria gonorrhoeae* in the United States established in 1986. Male urethral gonococcal isolates together with clinical and demographic patient data are submitted for susceptibility testing each month from STD clinics in approximately twenty-seven cities in the United States. GISP data demonstrate the ongoing spread of fluoroquinolone-resistance and the emergence of *N. gonorrhoeae* with decreased susceptibility to azithromycin in the U.S. GISP data are published in an annual report and periodically in the MMWR. (http://www.cdc.gov/std/gisp) contains GISP annual reports from 1998-2002 as well as important reference and link resources. | Ongoing. GISP data were used to revise the latest version of CDC's Sexually Transmitted Diseases Treatment Guidelines which were published in 2003. Data from 2003 will be available by Fall 2004. |
| CDC | Active Bacterial Core Surveillance (ABCs) | At Emerging Infections Program sites (EIPs), surveillance is conducted for invasive bacterial diseases due to pathogens of public health importance. For each case of invasive disease in the study population, a case report with basic demographic information is filed and, in most cases, bacterial isolates from a normally sterile site from patients are sent to CDC for laboratory study. System tracks emerging AR in isolates of *Streptococcus pneumoniae* , group A and group B streptococcus, and *Neisseria meningitidis* . Data provide an infrastructure for further research, such as special studies aimed at identifying risk factors for disease, post licensure evaluation of vaccine efficacy, and monitoring effectiveness of prevention policies. Program remains one of the most accurate and comprehensive surveillance tools available | Ongoing. ABCs produces yearly summaries on emerging resistance within the 10 EIPs (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee). An eleventh site, Texas, was added in 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| DoD | Surveillance for *Streptococcus pyogenes* among military trainees | Increasing resistance to macrolide antibiotics has been demonstrated for *S. pyogenes* isolates. Furthermore, during military-recruit training exercises, penicillin-allergic patients are often given erythromycin when mass prophylaxis is recommended. If resistant organisms are present or develop in this population, *S. pyogenes* infections (latent or overt) may not be treated effectively. Recruits could be reservoirs of resistant pathogens for military populations. This project conducts antimicrobial susceptibility and gene typing on *S. pyogenes* isolates collected from recruits at 9 military training centers and monitors for *S. pyogenes* resistance rates. As of September 2003, the rates detected were the following: erythromycin (13.5%), clindamycin (2.1%), tetracycline (4.6%), levofloxcin (1%) and 0% for penicillin and vancomycin. 2002 temporal trends in antibiotic resistance among *S. pyogenes* isolates demonstrated no discernible patterns, but increased resistance to erythromycin at 2 sites. | Reports of susceptibility test results and summary statements are being provided to primary care facilities, are accessible to DoD staff at www.geis.ha.osd.mil and have been used in presentations at national meetings. Generated data show moderate AR rates as of 2003. National DoD surveillance data for antibiotic resistance and emm gene type of group A streptococcal isolates from eight basic-training military sites was recently published in the Journal of Clinical Microbiology, Vol 48, October 2003. |
| DoD | Surveillance of antibiotic-resistant *S. pneumoniae* in military populations | Antibiotic resistance in S. pneumoniae has risen dramatically over the last decade, with varying levels of resistance found in different regions of the country. Similarly, S. pneumoniae causes significant morbidity among populations served by U.S. military medical centers. In this study, *S. pneumoniae* isolates from 7 U.S. military medical centers are serotyped, subtyped, and tested for antibiotic resistance. As of September 2003, full or partial penicillin resistance was found in 34% of the isolates, with 22% having resistance to three or more antibiotics. This represents no discernable change in rates from 2001 or 2002. Most invasive serotypes found in this population are included in the current 23-valent vaccine. | Reports of resistance findings and trends continue to be shared with the contributing medical centers, and summary statements are available through the website http://www.geis.ha.osd.mil. Continued surveillance is warranted for determining AR and type distribution trends over time in these populations, including association of particular strains with more invasive disease. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| DoD | Multilocus sequence analysis of *Streptococcus pneumoniae* isolates | DoD data from 1981 to 1991 suggest that *S. pneumoniae* may cause about 12% of military pneumonia hospitalizations. Multilocus sequence typing characterizes isolates of bacterial species using the sequences of internal fragments of 7 house-keeping genes. This highly discriminatory molecular typing method is used to track the global spread of virulence, to provide a direct comparison of isolates of multidrug-resistant *S. pneumoniae* , to define serotypes of isolates, estimate recombinational parameters, and identify discrete clonal complexes. | Ongoing. A pneumococcal isolate from a fatal case of meningitis was investigated using this technique, allowing the discovery of a non-vaccine serotype not commonly found among meningitis cases. During 2003 a conjunctivitis outbreak of *S. pneumoniae* was identified and analyzed. This work enabled the identification of a novel strain responsible for the outbreak and provided epidemiologic information on the causative isolate's resistance pattern. Further analyses of pneumococcal strains from Egypt is in process in hopes of providing valuable epidemiologic data for prevention and treatment options. Manuscripts of the above work have been submitted, and are under consideration for publication. |
| DoD | Surveillance of *Bordetella pertussis* among military trainees and the evaluation of newly developed highly sensitive PCR-based beacon probe for the detection of *B. pertussis* | Whooping cough is a contagious respiratory disease caused by *Bordetella pertussis* . Studies indicate that it is on the rise in adolescents, adults, and within confined populations such as military trainees. Surveillance for *B. pertussis* is established at 4 military training centers. Specimens are evaluated using PCR-based beacon probe. Standard culture, serology, and PCR results are compared to validate the accuracy of the PCR method. | Ongoing. As of March 2004, 360 specimen sets have been tested. Using culture, serology, and molecular testing, evidence of *B. pertussis* has been found in 10% of those enrolled. |
| DoD | Investigations of methicillin-resistant *Staphylococcus aureus* (MRSA) outbreaks occurring on military bases. | Hospital acquired MRSA outbreaks are well known, but recent reports have caused concern about community acquired MRSA infections. Investigations into this recent trend have been conducted at several military bases. Laboratory work has involved culture identification followed by antibiotic resistance testing. The presence of the panton valentine leukocidin gene which is a known virulence factor has been shown in many of these investigations. The multilocus sequence typing method has also been used to identify global virulent clones by characterizing the isolates with the sequencing of 7 house-keeping genes. Further molecular analyses have been utilized to discover the specific SCCmec type of these MRSAs, which is the mobile genetic element that mediates the methicillin resistance. | Ongoing. Capabilities are in-house when need arises. Historical samples from over the last decade are currently being analyzed. Trends in clones circulating before community acquired transmission was recognized are under investigation. Community acquired isolates are now being archived from various military settings. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| DoD | Investigation of multi-drug resistant *Acinetobacter baumanni* in US service members | *Acinetobacter baumannii* is an opportunist, with pathogenicity usually associated with high infectious doses or contamination of deep or necrotic wounds. Its importance as an nosocomial agent is due to its high rate of multi-antibiotic resistance. A review of *A. baumannii* infection in wounded US service persons is underway to determine 1) the number and location of patients involved, 2) what risk factors are common to the patients (eg, military unit or geographic proximity before injury, type and site of wound causing hospitalization, specimen source, type and location of all medical and surgical treatment, exposure to other patients with *A. baumannii* infection), and 3) the phenotypic strain(s) of *A. baumannii* involved. | Ongoing. Results of investigations are shared with preventive medicine and infectious disease staffs for review and implementation of prevention and control measures. |
| **Action Item #16: Provide Healthcare System Administrators and Other Decision Makers with Data on the Impact of Drug-Resistant Organisms (e.g., Outcome, Treatment Costs) and on Effective Prevention and Control Measures.** | | | |
| AHRQ | Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research. | The University of Pennsylvania Center for Education and Research on Therapeutics has undertaken studies on AR with the Veterans Affairs Medical Center in collaboration with Health Services Research and Development Service, Department of Veterans Affairs, and with hospitals in the Delaware Valley in collaboration with NIAID." | In hypothetical situations, the sicker the patient is, the more likely it is that a doctor will prescribe a new antimicrobial. This attitude is more prevalent among generalist physicians than among infectious disease subspecialists. (Metlay JP et al. Med Decis Making 2002;22:498-505.) |
| CDC | Grant program for Applied Research on Antimicrobial Resistance (AR): Estimates of Economic Cost for Antimicrobial Resistant Human Pathogens of Public Health Importance | This program will fund research for estimating the economic costs of antimicrobial resistance in human pathogens of public health importance and provide additional information needed to prevent and control AR. This will include: analysis of data on incidence, prevalence, and antimicrobial susceptibility of specific infectious diseases; development of methods to determine costs which are simple and reproducible for different antimicrobial resistant organisms; and calculation of economic costs (direct and indirect) of infections that are resistant to one or more antimicrobial agents compared with infections that are susceptible to those agents. | Awards to be made September 2004. |
| **Action Item #17: Expand and Enhance Coordination of Surveillance for Drug-Resistance in Enteric Bacteria In Sick and Healthy Humans and in Sick and Healthy Animals on Farms, at Slaughter, and at Retail.** | | | |
| FDA | Antimicrobial resistant bacteria in feed ingredients | Assess the prevalence of antimicrobial resistant bacteria in feed ingredients , primarily rendered product. This work will be done in conjunction with FDA field personnel when they inspect suppliers for compliance with the bovine spongiform encephalopathy (BSE) regulation. Results will be incorporated into NARMS. Expand NARMS into retail foods of animal origin. | Ongoing. Initial surveys (1 year) of rendered products and plant based proteins completed. Also, see item #2. In addition, see item #17, with regards to antimicrobial resistance bacteria from produce surveys. FDA is also collaborating with USDA to characterize antimicrobial resistance profiles of Salmonella and *E. coli* obtained from their annual produce survey. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #18: Evaluate the Usefulness of Monitoring Sentinel Human Populations (e.g., Farm, Abattoir, Fruit and Vegetable, and Food Processing Plant Workers) and Persons in the General Community for Infection or Colonization with Resistant Enteric Bacteria.** | | | |
| USDA | Transmission dynamics of antimicrobial resistance in integrated animal and human populations | This epidemiologic research will examine the influence of animal to human and human to animal contact on the transmission of resistant bacteria within a "closed" and integrated population of swine and humans. This research will be done in a human prison that raises, processes, and consumes swine. | Ongoing. H.M.Scott, Texas A&M University Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| FDA | Antimicrobial resistant bacteria in sentinel human populations | Evaluate abattoir workers for carriage of antimicrobial resistant bacterial pathogens. | Ongoing. Pilot study complete. |
| **Action Item #19: Conduct Pilot Studies To Assess the Extent of Environmental Contamination by Antimicrobial Drug Residues and Drug-Resistant Organisms That Enter the Soil or Water From Human and Animal Waste. If Contamination is Detected, Conduct Appropriate Surveillance in Waste, Surface and Ground Water, and Soil from Agricultural Areas in Which Waste Is Used for Fertilizer, and Conduct Studies To Determine Potential Impact on Human and Animal Health.** | | | |
| CDC | Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations | Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment. | Data published: Enzo R. Campagnolo, et. al. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. The Science of The Total Environment, Volume 299, Issues 1-3, Pages 89-95, November 2002. |
| CDC | Sampling for antibiotics in an agricultural river basin | Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities. | Report of preliminary findings is currently being reviewed and edited. More refined analysis of results for journal publication is in progress. |
| CDC | Evaluation of the impact of flooding on water quality and human health indicators | Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water. | Preliminary results presented at CDC CAFO workshop, Feb 2004. Some analysis still pending. |
| USDA | Transmission dynamics of antimicrobial resistance in integrated animal and human populations | See Action #18-This research is also sampling human wastewater access points and slaughter plant access points | Ongoing. H.M. Scott, Texas A&M University Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Determine the effectiveness of dairy manure composting on pathogen survival and subsequent environmental impact of composted manure used as soil amendments | A collaborative project between the USDA/ARS, FFSRU and the Texas Water Resources Commission is being conducted to examine antimicrobial susceptibility of pathogens and putative fecal coliforms isolated from dairy manure at various stages during composting and after land application. | Ongoing. Food and Feed Safety Research Unit, ARS College Station, TX. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Characterize Antimicrobial Resistance among *Pseudomonas aeruginosa* Isolates Recovered from Companion Animals, 1994-2003 | Observed rates of resistance to several antimicrobials merit sustained surveillance of bacteria isolated from companion animals to detect potential new emerging antimicrobial resistance phenotypes. In cooperation with the FDA, numerous *Pseudomonas aeruginosa* isolates recovered from companion animals across the U.S. from 1994-2003 are being evaluated for their susceptibility to veterinary and human use antimicrobials, including several fluoroquinolones. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Investigate longitudinal AR movement through closely linked animal and human environments | In collaboration with Texas A&M University, a three-year longitudinal observational study is being conducted to track multiple cohorts of animals, swine barn workers, slaughter plant workers and end-product consumers to determine transmission features reflecting the dissemination of strains of Salmonella and commensal *E. coli* isolated from these populations. This project will integrate molecular epidemiology, microbiology, mathematical biosciences, and population genetics, techniques to develop and empirically assess theoretical mathematical models pertaining to the transmission dynamics of single and multiple antimicrobial-resistant commensal and pathogenic bacteria in a multi-staged swine production system. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Enhance overall understanding of pathogens that pose a food-safety risk and to routinely monitor critical diseases in food-animal production | In response to growing surveillance needs, USDA-ARS, APHIS, and FSIS collectively developed CAHFSE to our understanding of pathogens that pose a food-safety risk by tracking them from farm to plant. The goal is to describe the prevalence of resistant bacteria and risk factors for their occurrence and to use this information to develop mitigation strategies. CAHFSE commenced in July 2003, and as of January 2004, fecal and blood samples are being collected from pigs on forty sentinel farms in four states, Minnesota, Iowa, Texas and North Carolina which are representative of swine production within the industry. Herd health/ management data are also being gathered. Currently, samples are being cultured for Salmonella, Campylobacter, *E. coli* and Enterococci, (zoonotic and commensal bacteria). Sera are being analyzed for antibody to *Lawsonia intracellularis* , the bacterium responsible for ileitis in growing swine. Slaughter/process sampling is expected to commence in 2004. | On going: This program is being expanded to all commodities and has been endorsed by the Animal Ag Coalition and other commodity groups. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Enhance overall understanding of pathogens that pose a food-safety risk and to routinely monitor critical diseases in food-animal production, and develop a model for future surveillance efforts on a national level. | CAHFSE will enable USDA to identify and implement mitigation strategies for animal health and food safety issues in a timely manner thereby averting adverse economic, animal well-being, and public health consequences. Further, it will provide comprehensive science based answers regarding animal health and public health, it will serve as a model for future surveillance efforts on a national level, and it will complement information obtained from both the National Antimicrobial Resistance Monitoring System (NARMS) and PulseVet programs. These data are being used by the swine industry to develop management recommendations for producers. | Ongoing: This program is being expanded to all commodities and has been endorsed by the Animal Ag Coalition and other commodity groups. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| **Action Item #20: Gather Information on the Relationship Between Antimicrobial Pesticide and Herbicide Use and the Emergence of Drug-Resistance by Monitoring.** | | | |
| **Focus Area II: Prevention and Control** | | | |
| **Action Item #21: Identify Factors That Promote or Impede Appropriate Drug Use in Hospitals, Extended Care Facilities, and Outpatient Settings In Collaboration with Partners.** | | | |
| AHRQ | Research Program Project (P01): Understanding and eliminating health disparities in blacks, project 2. | Economic access to antiretroviral (ARV) prescription drugs and adherence to ARV guidelines for African- American Medicaid enrollees with AIDS or HIV disease in South Carolina. | Ongoing. |
| AHRQ | Research Projects (R01): 1. Trial to reduce antimicrobial prophylaxis errors (TRAPE). 2. Improving antibiotic use In acute care settings. | 1. The trial will assess methods to avoid mistimed administration of preoperative antimicrobial agents. 2. Randomized controlled trial of a quality improvement program in urgent care clinics and emergency departments. | 1. Forty-four hospitals have been enrolled, and baseline data have been collected. The use of only a single prophylactic antimicrobial dose was found to be relatively uncommon. Randomized intervention and control groups have been selected. 2. Eight sites have been chosen, and there has been a training meeting for the research coordinators. A software program for chart abstraction for the specific requirements of the project has been developed to gather site-specific antibiotic prescription rates and practice patterns that will be examined and discussed with the physicians. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| AHRQ | Research demonstration and dissemination project (R18): HIV treatment error reduction using a genotype database. | This project is evaluating a computerized decision- support system that integrates HIV genotypic testing results with corresponding patient medication data within an electronic medical record system to reduce antiretroviral prescribing errors and improve antiretroviral drug selection. A second aim is to assess the efficacy and usability of this system in a community-based, outpatient setting serving a predominantly urban, minority, and low-income population. | Ongoing. |
| AHRQ | Mentored Clinical Scientist Development Award (K08): Antibiotic use and bacteriuria in the rural nursing home. | The focus of this work is antimicrobial resistance among gram-negative urinary isolates and the management of catheter-associated bacteriuria and urinary tract infections in rural nursing homes, where little is known about management practices, and surveillance is rarely performed. | Ongoing. |
| AHRQ | Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research. | The Harvard Pilgrim Healthcare CERT supports nine collaborating systems within an HMO Research Network to study antibiotic use in children. Between 1996 and 2000, there was a significant drop in the number of antimicrobials prescribed to children aged 3 months to 17 years. (Finkelstein JA et al. Pediatrics 2003;112:620-7.)" | Ongoing. |
| CDC | See Action Item #63 (Wisconsin Antibiotic Resistance Network). | See Action Item #63 (Wisconsin Antibiotic Resistance Network). | See Action Item #63 (Wisconsin Antibiotic Resistance Network). |
| CDC | See Action Item #63 (The Chicago Antimicrobial Resistance Network). | See Action Item #63 (The Chicago Antimicrobial Resistance Network). | See Action Item #63 (The Chicago Antimicrobial Resistance Network). |
| CDC | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). |
| FDA | Labeling Rule | The new labeling is intended to educate physicians and the public about the resistance problem and to encourage physicians to prescribe systemic antibacterial drugs only when clinically necessary. | The Final Labeling Rule was published in the Federal Register on February 6, 2003. The rule will go into affect February 6, 2004. |
| VA | Appropriate use of antimicrobials | The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federal agencies and other partners (including the private sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems. | Ongoing. Infectious Diseases Field Advisory Committee has representation on the national Antimicrobial Medical Advisory Panel (MAP) for pharmacy. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #22: Develop Appropriate Drug Use Policies and Evaluate the Impact (Including on Prescribing Patterns, Resistance Rates, Patient Outcomes, and Cost) of Implementing These Policies in Hospitals and Other Health Care Delivery Settings. Identify Ways To Increase Adherence to Appropriate Use Policies Proven To Be Beneficial in Collaboration with Partners.** | | | |
| AHRQ | Research Projects (R01): 1. Otitis media: parent education to avoid antibiotic use. 2. Pediatric EBM—getting evidence used at the point of care. 3. Minimizing antibiotic resistance in Colorado (MARC). | 1. Randomized clinical trial to evaluate the need for antibiotic therapy during an episode of mild acute otitis media. 2. Evaluation of whether use of an evidence-based decision-support system at the point of care will reduce frequency and duration of antibiotic therapy for otitis media and reduce duration of therapy for acute sinusitis. 3. Evaluation of the independent and combined marginal impact on antibiotic prescribing behavior and antibiotic resistance of two strategies for community education: (1) household- and office-based informational materials (small-scale community-based education) and (2) mass media (television, radio, print news, and Web site). | 1. Children experiencing painful acute otitis media with bullous myringitis may not be successful candidates for a watchful-waiting approach. (McCormick DP et al. Pediatrics 2003;112:982-6). 2. At three pediatric and family practice sites, evidence was presented at the point of care in an effort to improve physician behavior regarding the treatment of otitis media, allergic rhinitis, acute sinusitis, constipation, urticaria, pharyngitis, croup, and bronchiolitis. Preliminary findings are that, for all outcomes combined, the intervention group showed significant improvement in adherence to evidence-based recommendations. One manuscript describing barriers to point of care implementation is under review. 3. Antibiotics were prescribed at much higher rates than were recommended by CDC guidelines. The mass media campaign apparently led to fewer pediatric office visits for acute respiratory tract infections. This change does not appear to have been mediated by changes in knowledge or attitudes about appropriate antibiotic use, and the media campaign does not appear to have affected physicia |
| AHRQ | Small Research Grant (R03): Trial to reduce antibiotic use in a primary care Practice-Based Research Network (PBRN). | The Brigham and Women's Primary Care Practice-Based Research Network will design and implement an electronic medical record-based template for the care of patients with upper respiratory infections (URIs) in primary care practice, the URI Smart Set, and will test the implementation of the URI Smart Set in a randomized, controlled trial. The primary outcome will be antibiotic prescribing for URIs during a six-month period. | Data collection in progress. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| AHRQ | Independent Scientist Award (K02): Otitis media: parent education to avoid antibiotic use. | This study focuses on doctor-parent communication as a determinant of both inappropriate antibiotic prescribing and parent satisfaction with care. Parents presenting with their children who were suffering from cold symptoms were recruited for study participation. With informed consent, both physicians and parents were surveyed and their encounters were videotaped. The analyses of these data will involve an in-depth assessment of the patterns of communication between the physicians and parents observed in the 570 pediatric acute care encounters. The findings from this work will be used to develop a communication-based intervention to decrease antibiotic over prescribing in the pediatric outpatient setting. | Online commentary is physician talk that describes what the doctor notes during the physical examination. Online commentary that suggests that the findings are not problematic may provide an effective and efficient method for resisting perceived expectations to prescribe antimicrobials. (Mangione-Smith R et al. Soc Sci Med 2003;56:313-20.) |
| AHRQ | Collaborative Agreement (U01): PBRN--Safety New Antibiotic Prescription (SNAP). | In the Cincinnati PRBN parents of children with mild to moderate otitis media were given an antibiotic prescription but instructed not to fill it unless the child's symptoms worsened over the first 48 hours. | A subset of parents find a safety-net prescription and pain control acceptable in the treatment of acute otitis media, and antibiotic usage can be lowered with this strategy. (Siegel RM et al. Pediatrics 2003;112:527-31.) |
| AHRQ | Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research. | The University of Pennsylvania CERT has begun studies on improving the use of antibiotics locally and nationally, on reducing the use of antibiotics for acute bronchitis in outpatients, on the effect of formulary changes on the resistance patterns of *Escherichia coli* and *Klebsiella spp.* , on antibiotic-resistance patterns from outpatients with acne who are receiving tetracycline and a group of patients who are not, on antibiotic use and infection with drug-resistant *Streptococcus pneumoniae* in the United Kingdom, on risk factors for infection due to fluoroquinolone-resistant *E. coli* and *K. pneumoniae* , on risk factors for fluoroquinolone resistance in infections due to extended-spectrum beta-lactamase-producing *E. coli* and *K. pneumoniae* and on adherence to protease inhibitors and adherence to nonnucleoside reverse transcriptase inhibitors in HIV infection." | Of 100 patients who received fluoroquinolones in emergency departments, 81 received them outside of established guidelines. Of these 81 cases, 53% should have received a different antimicrobial, 33% had no evidence of infection, and 14% were not fully evaluated before receiving treatment. (Lautenbach E et al.A193 Arch Intern Med 2003;163:601-5.) |
| CDC | Get Smart: Know When Antibiotics Work | One strategy the Get Smart: Know When Antibiotics Work campaign utilizes to promote appropriate antibiotic use in the community is to provide funding to states and local communities to develop tailored campaigns. Although on a national level hand hygiene is currently not promoted, many of the state and local level sites have chosen to focus on preventing viral illnesses through proper hand hygiene. Campaigns in Michigan, Nevada, and Minnesota have developed educational materials and/or trainings on the basics of hand hygiene in various settings. | Hand washing campaigns on the state and local level to promote the transmission of viral illnesses are currently funded and being implemented in six sites. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Evaluation of routine cycling of antimicrobial agents | Routine cycling in the choice of empiric antimicrobial agents has been proposed as a means of limiting development of AR mutants in hospitalized patients. This study in medical intensive care units at 3 institutions evaluates changes in prevalence of resistant target pathogens and patient outcomes during cycling interventions compared to baseline. The results will indicate whether cycling interventions have a protective effect on infection or colonization with resistant target pathogens and the impact of specific cycling periods on adequate therapy for suspected infections, length of hospital stay, and mortality rates. | Data collection and isolate processing is complete. Preliminary results suggest cycling of agents are ineffective to reduce targeted resistance among gram-negative isolates. Reporting of results and suggested measures for further study or consideration for hospitals considering cycling are in progress, expected Summer 2003. Two manuscripts in press: Merz LR, Warren DK, Kollef MH, Fraser VJ. The Effects of an Antibiotic Cycling Program on Antibiotic Prescribing Practices in an Intensive Care Unit. Antimicrobial Agents and Chemotherapy Aug 2004;48(8) (in press). Warren DK, Hill HA, Merz LR, Kollef MH, Fridkin SK, Hayden MK, Fraser VJ. Cycling Empiric Antimicrobials to Prevent Emergence of Antimicrobial-Resistant Gram-Negative Bacteria among Intensive Care Unit Patients. (Critical Care Medicine, in press) |
| CDC | See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings). | See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings). | See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings). |
| CDC | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). |
| CDC | See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections). |
| CDC | See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP). |
| FDA | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). |
| VA | See Action Item #21. | See Action Item #21. | See Action Item #21. |
| **Action Item #23: Evaluate the Relationship Between Prescribing Behavior and Specific Antimicrobial Drug Marketing and Promotional Practices. Assess the Public Health Effects of These Practices in Collaboration with Partners.** | | | |
| FDA | Direct to Consumer (DTC) Promotion | Review “Direct to Consumer” (DTC) promotion as applies to antimicrobials. | Ongoing. |
| **Action Item #24: Help Individual Hospitals and Healthcare Systems Analyze How the Availability of AR Data and Computer-Assisted Decision Support Systems Influences Prescriber Behavior, Health Outcomes, and Costs. This Plan May Include the Provision of Computer Software and the Establishment of Projects That Involve the Medicare Peer Review Organizations (PROs).** | | | |
| CDC | See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). | See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy). |
| VA | Emerging Pathogens Initiative (EPI) | Data on antimicrobial resistance with quartile rankings in the VHA nationwide are provided to the Networks, including reporting site-specific data by using the EPI, an automated surveillance system. This will be an ongoing initiative since it is not entirely clear what the best method for AR feedback will be in the final analysis. | Ongoing at VA sites across the country. Enhancements that will acquire additional information on antimicrobial resistance of specified organisms are anticipated to be distributed to reporting stations by July 1, 2004. |
| **** TOP PRIORITY ****<br>**Action Item #25: Conduct a Public Health Education Campaign To Promote Appropriate Antimicrobial Use as a National Health Priority. The Health Campaign Should Involve Many Partners.** | | | |
| CDC, FDA | "Get Smart: Know When Antibiotics Work" national ad campaign. | This national media education campaign is being developed to promote appropriate antimicrobial drug use in the community for upper respiratory infections, e.g., to decrease patient requests for antibiotics for illnesses for which they offer no benefit. Target audiences are parents of young children and healthy adults. The campaign will use a variety of health communication materials based on concepts tested in focus groups, and its effectiveness will subsequently be evaluated. | Ogilvy Public Relations Worldwide was awarded the media contract in September 2001 to implement a three phase media plan. Phase I focused on research and development while Phase II culminated with a nation-wide launch of the media campaign. As a result of the September 2003 launch a steadily increasing audience of over 100 million has been reached through television, print, and online media. Public awareness of the Get Smart campaign increased as well as evidenced by a nearly 200% increase hits to the campaign Web site since September 2003. Phase III of the media plan involves continuing the outreach efforts implemented in Phase II. During the final phase of the media plan the campaign will test and develop appropriate antibiotic use messages and media for Spanish speaking Latino parents of young children and English speaking healthy adults 21- 49, in an effort to expand the campaign's reach. This work will be conducted during 2004 and will be completed by May 2005. |
| CMS | National Surgical Site Infection Campaign - Promotes Appropriate Use of Surgical Prophylaxis | CMS is conducting a national campaign to promote the selection of appropriate antibiotics for surgical infection prophylaxis and to limit the duration of prophylaxis to 24 hours. | Ongoing. All 53 Quality Improvement Organizations are active in this effort. There is a supporting website at www.qualityhealthcare.org/ihi/Topics/PatientSafety/SurgicalSiteInfections/ |
| CDC | See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare). | See Action Item #26. | See Action item #26. |
| FDA | See Action Item #23 (Direct to Consumer (DTC) Promotion). | See Action Item #23 (Direct to Consumer (DTC) Promotion). | See Action Item #23 (Direct to Consumer (DTC) Promotion). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **** TOP PRIORITY ****<br>**Action Item #26: In Collaboration with Many Partners, Develop and Facilitate the Implementation of Educational and Behavioral Interventions That Will Assist Clinicians in Appropriate Antimicrobial Prescribing.** | | | |
| AHRQ | Mentored Clinical Scientist Award (K08): shared decision-making and inappropriate antibiotic use. | The recipient will develop and validate an instrument to measure shared decision-making in pediatric primary care. This instrument will then be used in a cross-sectional study to examine the relationship of shared decision-making to quality of care outcomes for children's upper respiratory infections. The candidate hypothesizes that shared decision-making in acute primary care visits for upper respiratory infection will decrease inappropriate antibiotic prescribing, while preserving visit satisfaction. | The development and validation of an instrument to assess shared decision-making in pediatric primary care is in progress. Data collection for this effort has been completed, and the coding of videotapes is proceeding. A manuscript is under review.. |
| CDC | Campaign to prevent antimicrobial resistance in healthcare settings | This campaign focuses on preventing AR in healthcare settings, such as hospitals and long-term care facilities. An evidence-based 12-step program promotes four strategies for clinicians: 1) preventing infection, 2) diagnosing and treating infection effectively, 3) using antimicrobials wisely, and 4) preventing transmission. Variations of the 12 steps will be tailored to specific patient populations (e.g., dialysis, surgery, geriatrics, critical care, obstetrics, emergency care, pediatrics, and patients in long term care facilities). When these strategies are fully implemented and evaluated, improvements are anticipated in infection control, appropriate antimicrobial drug use and incidence of drug-resistant infections occurring in healthcare settings. | Established partnerships with Infectious Diseases Society of America (IDSA) and American Society of Microbiology (ASM) to disseminate campaign messages; developed initial educational materials for clinicians; created website; rolled out campaign and launched a 12-step campaign specifically for dialysis patients in 2002. Design of 12-step campaign for preventing AR in surgery patients is underway utilizing collaborations with the American College of Surgeons (ACS) and the Surgical Infection Society (SIS), as well as a campaign for hospitalized children. Launch of both is expected this Fall 2003. Several health communication tools were developed and disseminated to various health systems including brochures, slide sets, posters, pockets cards, and badge. Four institutions in Pittsburgh piloted the campaign materials and conducted an evaluation. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections | The campaign assists states in implementing broad-based multi-faceted health communication and behavioral interventions to promote appropriate antibiotic use for outpatient upper respiratory infections. State health departments develop broad-based coalitions (e.g., state medical societies, healthcare delivery organizations, healthcare purchasers, consumer groups), use CDC educational materials, develop materials of their own, launch campaigns targeting providers and the general public , and evaluate various aspects of their local campaigns and/or appropriate antibiotic use knowledge, behaviors, and attitudes . Controlled trials have demonstrated success of this program in decreasing inappropriate prescribing; also, nationwide antibiotic prescribing rates for children are declining. | Ongoing in twenty-eight states.<br>Get Smart maintains a comprehensive Web site funded sites can utilize to gain access to campaign resources and educational tools and to learn more about national campaign activities.<br>The Get Smart campaign is developing an evaluation manual for state partners as a guide for developing and implementing impact and/or outcome which will be released in 2004.<br>In June 2003, Get Smart hosted its fourth national conference, "Expanding Our Vision: CDC and Partners' National Conference on Appropriate Antibiotic Use in the Community". The conference brought together over 200 p |
| CDC | Partnerships with healthcare delivery organizations and insurers to promote the appropriate use of antibiotics for outpatient upper respiratory infections | Work with Coalition for Affordable Quality Healthcare to implement educational and behavioral interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections in managed care organizations. | Ongoing. Continued projects in twenty-six organizations, with 131 million members in 2002.<br>Implemented CME certification programs for healthcare personnel participating in educational programs.<br>In collaboration with the Council for Affordable Quality Healthcare the Get Smart campaign implemented an online CME certification program for healthcare personnel. Since September 2004 over 900 healthcare personnel have completed the program. |
| CDC | A medical curriculum promoting appropriate use of antibiotics | Topics include extent of antibiotic resistance, diagnostic techniques, and appropriate antibiotic use. Case studies focus on examination, diagnosis, treatment, and communication. This course is designed to meet the needs of a variety of medical schools with components that can be used separately or as a whole. | Ongoing. CDC and the University of California, San Diego developed and produced a multi-faceted educational curriculum throughout 2000 and 2001. During 2002 CDC, in collaboration with the Association of American Medical Colleges, recruited six medical schools to pilot test the medical school curriculum during the 2002-2003 school year. The curriculum was rated favorably by both students and medical school administrators. Using the data received from the pilot tests, revisions and updates were made and a final version of the curriculum is scheduled to be released for adoption in 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Reporting antimicrobial susceptibility data to clinicians | Assist NCCLS to produce guidelines for clinical microbiology labs on how to compile and report summaries of cumulative antimicrobial susceptibility data (antibiograms) in a standardized manner to aid in clinical decisions. When completed and evaluated, standard reports should improve empiric prescribing, based on data of antimicrobial susceptibility testing and allow comparisons of data among hospitals. | Ongoing. Developed guidelines in 2001. Multicenter study showed significant problems in reporting of antimicrobial susceptibility testing results of positive blood cultures. Educational programs to improve reporting practices are now in progress in multiple healthcare institutions |
| CMS | Surgical Care Improvement Project also see Action Item # 25 (National Surgical Site Infection Initiative) | All 53 QIOs are working with volunteer hospitals in their jurisdiction and are partnering with Federal and non-Federal agencies and Professional Organizations to look at processes and outcomes involving timing, duration, proper drug selection, surgical site preparation, and post-op complications including pneumonia and surgical infection. | This project will continue into the QIOs next scope of work. |
| FDA | See Action Item #23 (Direct to Consumer (DTC) Promotion). | See Action Item #23 (Direct to Consumer (DTC) Promotion). | See Action Item #23 (Direct to Consumer (DTC) Promotion). |
| FDA | See Action Item #25 (Education/Outreach Plan) . | See Action Item #25 (Education/Outreach Plan) . | See Action Item #25 (Education/Outreach Plan) . |
| VA | Prudent use of antibiotics interventions | The VHA is already involved in many of these activities with particular emphasis on educational activities and training for prescribers at all levels, including physicians, nurse practitioners, and others who are involved with the direct care of patients. Particularly, the VHA provides a strong role in education for health professions students, medical and nursing trainees, and others critical to the provision of care to patients such as social workers, psychologists, and advanced role nurses. In addition, the VHA has produced guidelines, including those that relate to antimicrobial drug use. Therefore, the VHA is well underway for this action item. | Ongoing. |
| **Action Item #27: Explore Ways To Integrate Appropriate Use Information into Antimicrobial Package Inserts and Promotional Materials, To Provide Such Information to Patients with Each Prescription, and To Provide Clear Guidance to Industry To Ensure That Promotion of Antimicrobials Directed Towards Consumers Encourages Appropriate Use and Discourages Inappropriate Use.** | | | |
| FDA | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). |
| **Action Item #28: Articulate Factors That Support the Current Approach of Requiring Prescription-Only Dispensing for All Systemic (e.g., Nontopical) Antimicrobial Drugs Used In Clinical Medicine.** | | | |
| **Action Item #29: Periodically Review and Update Antimicrobial Drug Susceptibility Information Including In Drug Labeling, with Input from Stakeholders and Other Experts, e.g., the National Committee for Clinical Laboratory Standards (NCCLS) and CDC.** | | | |
| FDA | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #30: Convene an Advisory Panel or Other Expert Group in Involving Stakeholders and Partners To Consider Issues Related to Resistant Pathogens That Cause Serious Infections for Which Available Treatments Options Are Very Limited or Nonexistent.** | | | |
| FDA, CDC, NIH | Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP) | Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues. | Workshop held April 15-16, 2004. |
| FDA | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). | See Action Item #21 (Labeling Rule). |
| FDA | Otitis Media Advisory Committee | Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population). | Meeting held on July 11, 2002. |
| FDA | FDA/PhRMA Co-Sponsored Workshop | Discussion of statistical issues in clinical trials including trials related to resistant pathogens. | Meeting held on November 9, 2002. |
| FDA | FDA/IDSA/PhRMA Co-Sponsored Public Workshop | Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical Research and Manufacturers of America, and U.S. academic institutions along with representatives from CDC and NIH to address current topics of interest associated with AR and antimicrobial drug development. | Meeting held on November 19-20, 2002. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of issues relating to macrolide-resistant Streptococcus pneumoniae *(* MRSP) | Meeting held on January 24, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of issues relating to AR in *Streptococcus pneumoniae* . | Meeting held on March 4, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant pathogens. | Meeting held on May 5, 2003. |
| FDA | FDA/NIAID Co-Sponsored Public Workshop | Coordinated a public workshop with the National Institute of Allergy and Infectious Diseases, which brought together top scientists to discuss issues affecting antifungal drug development for febrile neutropenia and combination antifungal therapy. | Meeting held on September 4, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of clinical trial design issues for demonstrating the safety and efficacy of antibacterials in the treatment of diabetic foot infections. | Meeting held on October 28, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of clinical trial design issues for studies in acute bacterial sinusitis. | Meeting held on October 29, 2003. |
| **Action Item #31: Convene A Working Group To Examine the Impact of Federal Reimbursement Policies for Home Parental Antimicrobial Treatment, Appropriate Antimicrobial Use, and Appropriate Use of Antimicrobial Susceptibility Testing. Where Needed, the Working Group Will Make Recommendations for Modifying These Policies.** | | | |
| **Action Item #32: Develop and Submit Measures for Appropriate Antimicrobial Use to the National Committee for Quality Assurance for Inclusion in Health Plan Employer Data and Information Set (HEDIS), Which Provides Comparative Data on Managed Care Organizations** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Development and testing of HEDIS measures for appropriate antibiotic use | In this project, CDC epidemiologists collaborate with experts in the development and testing of HEDIS measures to develop and test one or more measures of appropriate antimicrobial use in children. Measures include rate of prescribing antimicrobial drugs for acute upper respiratory infections and bronchitis; rate of prescribing antimicrobial drugs for pharyngitis where no throat culture or rapid streptococcal antigen test was performed; and episodes of otitis media treated with a recommended first-line agent. When the measure is incorporated into HEDIS, the measure and its impact on physician and patient awareness of appropriate antimicrobial use will be evaluated. | Ongoing. Awarded contract in 2001 to Association of American Medical Colleges. During 2002 CDC, in collaboration with the Association of American Medical Colleges, recruited medical schools to participate in a pilot testing of the medical school curriculum. Results from the pilot will help in the development of appropriate evaluation tools, in the evaluation of the curriculum in terms of acceptability of the material and feasibility of implementation, and marketing to appropriate target audiences, and in final revisions.<br>In 2002, National Center for Quality Assurance (NCQA) was presented with specifications for two potential measures relating to Appropriate Antibiotic Prescribing for Respiratory Infections for Children. Two measures were agreed upon, developed and tested following NCQA's specifications. In 2003 these two measures; one on pharygitis and one on upper respiratory infections were pilot tested. NCQA reviewed and accepted these measures and they were incorporated into the 2004 HEDIS |
| **Action Item #33: Evaluate The Potential Impact Of Improved Diagnostic Tests, Including Rapid Point-of-Care Tests on Antimicrobial Drug Use and Patient Care, and Assess Their Financial Implications. Take into Account Tests That Distinguish Between Bacterial and Viral Infections, Tests That Identify Resistant Pathogens, and Tests That Distinguish Common Clinical Entities such as Bacterial Sinusitis and Acute Bacterial Otitis Media from Illnesses with Similar Manifestations for Which Antimicrobials Are Not Beneficial.** | | | |
| AHRQ | Small research grant (R03): a diagnostic decision aid for pediatric sinusitis. | Investigators at the University of Washington are exploring whether use of a diagnostic decision aid that is completed by parents in the waiting room prior to being seen can assist providers in more accurately diagnosing sinusitis and thereby diminish inappropriate antibiotic use. | To date 546 patients have been enrolled. Preliminary results indicate 1/5 of patients presenting to the clinic with cough/cold symptoms met criteria for sinusitis, and 1/3 of all patients met the CDC criteria for high dose amoxicillin. Also, 2/5 of patients presenting with cough/cold symptoms were prescribed antimicrobials. |
| AHRQ | Research career award (K08): randomized trial of sinus CT for acute sinusitis. | This investigator at the University of Washington will develop and implement of a randomized controlled study assessing the impact of sinus CT on the use of antibiotics for patients with acute sinusitis. She will also develop and validate clinical prediction rules through the randomized clinical trial. | Awarded in 2004. |
| CDC | Rapid detection of MRSA colonization to reduce spread within hospitals | This project's focus has been revised to study the dynamics of MRSA transmission in the ICU setting. This information will the be used to institute appropriate infection control measures to decrease the spread of MRSA in high-risk hospital areas. | Ongoing. Continued patient enrollment in 2003. Samples have been collected and stored to determine strain transmission. Genetic analysis of samples is underway with results expected in 2004. |
| **Action Item #34: Identify Economic and Other Barriers in the Health Care System (e.g., Reimbursement Policies by Third Party Payers, Managed Care Practices, Cost Considerations, Empiric Treatment Recommendations, etc.) to Diagnostic Testing That Promotes Appropriate Use of Antimicrobials. Develop Recommendations That Remove Disincentives or Promote Incentives to Such Testing.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| VA | Laboratory accreditation | The VHA currently participates in surveys by the College of American Pathologists and all VHA laboratories are appropriately credentialed. | Ongoing. |
| **Action Item #35: In Collaboration With Professional Societies, Industry, Health Departments, And Other Stakeholders And Partners, Develop Guidelines for Clinicians And Clinical Microbiology Laboratories To Address Appropriate Specimen Collection, Interpretation, And Reporting Of Susceptibility Tests, And Use Of In-Office Tests For Infection.** | | | |
| CDC | National laboratory system demonstration projects | These projects promote linkages and coordination between State Public Health and clinical microbiology laboratories to optimize laboratory practice, in collaboration with medical societies and other stakeholders. AR is a major focus area. Example: In one project, the State of Washington developed and distributed a survey of laboratory practices related to antimicrobial susceptibility testing (AST) and has provided training to approximately 2,000 laboratorians in a dozen states in quality control for AST testing through a teleconference and a train-the trainer program on using an interactive CD-ROM program on the NCCLS AST laboratory guidelines. The survey will then be re-administered to measure changes in practice and use of the guidelines. | Ongoing. CDC-funded demonstration projects are underway in numerous states. MASTER is an acronym for Multi-level Antimicrobial Susceptibility Testing Educational Resources. Periodic updates on the website provide case studies addressing contemporary testing issues, questions and answers for users, a review of recent papers that have implications for testing and reporting, other new information, and lists of reference materials including books, and links to other websites. |
| CDC | Grant Program: Applied Research on Antimicrobial Resistance - Validation of National Committee for Clinical Laboratory Standards (NCCLS) Breakpoints for Bacterial Human Pathogens | The purpose of the program is to provide assistance for applied research aimed at prevention and control of the emergence and spread of AR in the United States. This program will focus on validation of NCCLS breakpoints for bacterial human pathogens of public health importance. This research includes three components that will provide information needed to prevent and control AR: (1) validating existing interpretive criteria for pathogens of public health importance; (2) developing new interpretive criteria for pathogens of public health importance using existing NCCLS methods and quality control; and (3) developing new interpretive criteria and new antimicrobial susceptibility testing methods for pathogens of public health importance using existing NCCLS methods and quality control as a starting point for novel test development. | Funded three programs in the Fall of 2002: University of Texas Medical Center, (Development of Interpretive Breakpoint Criteria for Neisseria Meningitidis); University of Pittsburg, (NCCLS Interpretive Criteria for Salmonella); University of Wisconsin Medical Center, (Validation of NCCLS Methods and Breakpoints for Extended Spectrum beta-lactamases). |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CMS | Memo to Proficiency Testing (PT) Providers | In an April 7, 2004 letter to Proficiency Testing (PT) Providers, CMS is requesting all PT providers offering bacteriology to include educational material discussing antimicrobial selection and testing for 2004. During 2005, labs are asked to identify antimicrobial agents and laboratory tests or reports that are inappropriate by NCCLS guidelines, with no penalty attached. Beginning in 2006, inappropriate drug choices will be graded as incorrect results. The PT programs are to use the NCCLS guidelines (M100-S14 Performance Standards for Antimicrobial Susceptibility Testing: Fourteenth Informational Supplement) regarding proper selection of antimicrobial agents for testing and reporting. | Letter distributed 4/7/2004. |
| CDC | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). | See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections). |
| **Action Item #36: In Collaboration with Professional Societies, Industry, Health Departments, and Other Stakeholders, Develop Guidelines That Address the Use of Clinical Microbiology Laboratories for Use by Health Care Delivery Organizations.** | | | |
| CDC | Guidances for stool sample testing by clinical laboratories | CDC's FoodNet co-authored a paper on guidelines for stool sample testing by clinical laboratories. | Wallace DJ, Van Gilder T, Shallow S, Fiorentino T, Segler SD, Smith KE, Shiferaw B, Etzel R, Garthright WE, Angulo FJ, and the FoodNet Working Group. Incidence of Foodborne Illnesses Reported by the Foodborne Diseases Active Surveillance Network (FoodNet)-1997. Journal of Food Protection 2000; 63 (6): 807-809. |
| **Action Item #37: Promote the Increased Performance of Direct Examination of Microbiological Specimens (e.g., by Gram Stain or Other Rapid Method) in Circumstances Where Appropriate, Clinically Relevant, and Reliable Information Can Be Garnered, as Readily Available Point-of-Care Diagnostic Test. This Step Will Require Working Within the Framework of the Clinical Laboratory Improvement Amendment (CLIA) Regulations and Involving Medical Education And Health Care Delivery Organizations.** | | | |
| **Action Item #38: Identify Factors That Promote Transmission of Drug-Resistant Pathogens in Healthcare Facilities, in Extended Care Facilities, and in Community Settings, Including Daycare Centers in the Community at Large. These May Include Characteristics of the Facilities and of the Populations They Serve.** | | | |
| CDC | Grant Program for Applied Research on Antimicrobial Resistance: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use | Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings. | Ongoing. Three three-year awards were made in 2001. Research areas included AR among *E. faecium* in animal and human populations and fluoroquinolone resistance among *E. coli* in healthcare settings. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Grant Program for Applied Research on Antimicrobial Resistance: Characterization of Strains of Community-Associated Methicillin-Resistant *Staphylococcus aureus* | This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus (S. aureus)* causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques. | Five three years awards were made in 2003. Recipients are Harbor-University of California Los Angeles Research & Education Institute, University of California – San Francisco, University of Chicago, and William Beaumont Hospital. " |
| CDC | Antimicrobial resistance in *Staphylococcus aureus* and *Streptococcus pneumoniae* among Alaska Natives | CDC is conducting surveillance and evaluation of prevention and control measures for MRSA skin infections, community-wide surveys for carriage of penicillin-nonsusceptible *Streptococcus pneumoniae* , and surveys on antimicrobial drug use. These activities will provide knowledge of MRSA prevalence and effectiveness of prevention measures, assist with the development of treatment guidelines for community-onset MRSA infections, assess the effect of the new pneumococcal vaccine on resistant pneumococcal infections, and assess the effect of education on appropriate antimicrobial agent use in Alaska. | Population based surveillance for invasive *Streptococcus pneumoniae* in Alaska has documented a 90% decline in disease due to types found in the infant conjugate pneumococcal vaccine (PCV7) since it's introduction in 2001. A corresponding decrease in invasive antimicrobial pneumococcal infections has been seen for all drug classes tested. Nasopharyngeal colonization studies have shown decreases in carriage of PCV7 types among children and adults with a decline in colonization of antimicrobial resistant pneumococcus. These decreases have been greatest among fully vaccinated children but are apparent also for partially vaccinated children and adults who live with vaccinated children. These data indicate that the vaccine has some impact on carriage even among less-than-fully vaccinated persons and an indirect effect on household contacts. |
| CDC | See Action Item #39 (Centers of Excellence in Healthcare Epidemiology). | See Action Item #39 (Centers of Excellence in Healthcare Epidemiology). | See Action Item #39 (Centers of Excellence in Healthcare Epidemiology). |
| CDC | See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP). | See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP). |
| CDC | See Action Item #63 (The Wisconsin Antibiotic Resistance Network). | See Action Item #63 (The Wisconsin Antibiotic Resistance Network). | See Action Item #63 (The Wisconsin Antibiotic Resistance Network). |
| **** TOP PRIORITY ****<br>**Action Item #39: Evaluate the Effectiveness (Including Cost-Effectiveness) of Current and Novel Infection-Control Practices for Health Care and Extended Care Settings and in the Community. Promote Adherence to Practices Proven To Be Effective.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Centers of excellence in healthcare epidemiology (Prevention Epicenters) | Academic medical centers conduct research to improve infection control practices. Current projects address prevention of infections related to central vascular catheters and surgical site and bloodstream infections. A substantial proportion of these infections are drug-resistant. Reduction of these infections would also reduce antimicrobial use in healthcare settings, thus decreasing the environmental pressure favoring development and spread of resistant infections. | Awarded funds to seven academic medical centers for research projects. 2003 accomplishments include: 1) the development and testing of a more efficient and sensitive method for SSI surveillance defined by antimicrobial exposure exceeding a procedure-specific number of days together with diagnosis codes; and 2) creation of antimicrobial management teams at 5 Epicenters to improve antimicrobial therapy choices at their institutions. Continued multicenter study to evaluate the effectiveness of antimicrobial management based on review of therapy after 48 hours. The data collection will be completed in FY2004 and data analysis will begin. |
| CDC | See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities, | See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities, | See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities. |
| VA | A. Six Sigma process to promote hand hygiene in VA medical facilities. B. Antibiotic Resistance Patterns for Streptococcus pneumoniae in VA. C. Antibiotic Resistance and Extended Spectrum Beta-lactamase (ESBL) Activity in VA: A Two-year Review. | A. National VA effort to use the Six Sigma process in the hand hygiene promotion effort. Pilot project at 3 VA medical facilities, with products from the testing to be distributed nationwide to all VA medical facilities. B. *S. pneumoniae* laboratory data collected nationwide from VA medical facilities to identify antibiotic resistance patterns. C. Antibiotic resistance and ESBL activity data collected from VA medical facilities nationwide. | A. Six Sigma process regarding hand hygiene being tested at 3 VA medical facilities. B. Abstract presented at the Annual Conference on Antimicrobial Resistance, June 23-25, 2003, Bethesda, MD. Authors: G Roselle, A Kelly, L Danko, L Simbartl, S Kralovic. C. Abstract presented at the International Conference on Emerging Infectious Diseases, 2004, Feb 29-Mar 3, 2004, Atlanta, GA. Authors: GA Roselle, SM Kralovic, LH Danko, LA Simbartl, LB Rice. |
| **Action Item #40: Evaluate the Cost-Effectiveness and Impact on Patient Care and Drug Resistance of Medical Devices That Incorporate Anti-Infective Compounds To Prevent Infection (e.g., Anti-Infective Urinary Catheters and Prosthetic Heart Valves). Where Appropriate (e.g., Shown To Be Effective and Not Induce Resistance), Encourage the Clinical Use of These Devices.** | | | |
| FDA | Devices containing antimicrobials – draft guidance | Draft guidance document for industry: how CDRH intends to regulate devices containing antimicrobial drugs, and what information regarding efficacy and resistance CDRH wants to see in premarket applications (interim until rulemaking is completed) | In development. |
| FDA | Standards development seminar | Standards development: seminar to gather information from experts on developing test methods that should/could be used to demonstrate efficacy of antimicrobial agents on devices for use in guidance and rulemaking. | Seminar held on December 3-4, 2001. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #41: Encourage the Development and Implementation of Clinical Alternatives to Those Invasive Medical Procedures That Increase the Risk of Infection in Hospitals and Other Health Care Settings, e.g., Substitutions of Transcutaneous Monitoring of Blood Oxygen Levels of Indwelling Catheters.** | | | |
| **Action Item #42: Evaluate the Benefits and Risks of Incorporating Antimicrobial, Disinfectant, or Antiseptic Chemicals into Consumer Products (e.g., Soap, Toys, Kitchen Utensils, Clothes, Paints, Plastics, and Film Preservatives) and of Applying Disinfectants and Sanitizers to Hard, Non-porous Surfaces such as Food-Contact Surfaces, Hospital Premises, Bathrooms, etc. Consider Whether They Have Any Efficacy in Reducing and/or May Play a Role in Promoting Drug Resistance.** | | | |
| **Action Item #43: Conduct a Public Health Campaign To Promote Hand Hygiene and Other Hygienic Practices, as well as Other Behaviors That Prevent the Transmission of Infectious Organisms, in Collaboration with Professional Societies and Stakeholders. This Campaign May Be Coordinated with the Public Health Education Strategy To Promote Appropriate Antimicrobial Use Described in Action Item #25: Prevention and Control.** | | | |
| CDC | Get Smart: Know When Antibiotics Work | One strategy the Get Smart: Know When Antibiotics Work campaign utilizes to promote appropriate antibiotic use in the community is to provide funding to states and local communities to develop tailored campaigns. Although on a national level hand hygiene is currently not promoted, many of the state and local level sites have chosen to focus on preventing viral illnesses through proper hand hygiene. Campaigns in Michigan, Nevada, and Minnesota have developed educational materials and/or trainings on the basics of hand hygiene in various settings. | Hand washing campaigns on the state and local level to promote the transmission of viral illnesses are currently funded and being implemented in six sites. |
| CDC | "It's a SNAP" handwashing campaign | CDC is collaborating with the Soap and Detergent Association to launch the second year of an education-based effort for middle level school communities to improve health by making hand cleaning an integral part of the school day. | Ongoing. Vist SNAP at: http://www.itsasnap.org/index.asp |
| **Action Item #44: Facilitate and Support the Activities of Infection Control Programs in Health Care Settings as a Component of Medical Care. Promote Infection Control Education at all Stages of Training and Practice for all Health Care Workers Who Have Contact with Patients.** | | | |
| CDC | Division of Healthcare Quality Promotion (DHQP), National Center for Infectious Diseases (NCID) | DHQP, formerly known as the Hospital Infections Program, has in its mission surveillance, applied research, and prevention and control of infections in healthcare settings. | Numerous ongoing projects in collaboration with partners. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| VA | Educational activities since January 2001: A. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August 8, 2001. B. Emerging Pathogens Satellite Broadcast, September 5, 2001 C. Infomercials taped and aired on VA Knowledge Network. Viewed by VHA employees. D. Infection: Prevention and Containment Conference, such as handouts and responses to questions posed by attendees. E. Memorandum "CDC Hand Hygiene Recommendations and JCAHO Patient Safety Goal 7 for 2004" from VA Under Secretary for Health F. National Center for Health Promotion and Disease Prevention Monthly Topics | Conference Speakers/Topics: A. Employee Health: Vaccine and PPD Issues. Speaker: Gary A. Roselle, M.D. Emerging Infectious Diseases. Speaker: Stephen M. Kralovic, M.D. B. Part 1 – Tuberculosis. Part II – Implementation Thoughts and the Future. Presenter: Gary A. Roselle, M.D. C. 2-3 minute "infomercials" covering issues relating to influenza, PPD's and bloodborne pathogens. D. Conference Speakers for Infection: Prevention and Containment Conference included Gary A. Roselle, M.D., Stephen M. Kralovic, M.D., Robert Gaynes, M.D., Louis Rice, M.D., Robert Muder, M.D., Lynne Sehulster, PhD. E. The memorandum addressed the VA expectations concerning hand hygiene in VA medical facilities. F. Some of the monthly topics address specific diseases and some address specific infectious diseases preventive measures | The VHA is currently in the forefront of infection control programs in the healthcare settings in the U.S. This includes national guidance, educational activities, and current financial support of the program nationwide. It is anticipated that such activities will continue, particularly because of the more recent emphasis on patient safety and infection control as part of an overall safety program to prevent excess infections in the healthcare setting. D. Infection: Prevention and Containment Conference was held May 4-6, 2004. E. VA Under Secretary for Health Memorandum pertaining to hand hygiene was issued to VA medial facilities nationwide 12/15/03. F. Information on the following, STDs/AIDS (April 2003), Immunizations (August 2003), and Tuberculosis (March 2004) were issued to VA facilities nationwide |
| **Action Item #45: Support Ongoing Public Health Education Campaigns on Food Safety, such as FDA and USDA's Fight BAC Program, Whose Aims Are To Educate Food Producers, Retailers, and Consumers About Food Safety Practices That Reduce Foodborne Infections (Including AR Infections).** | | | |
| CDC, USDA, FDA | Children Fight BAC!: A Scientific, Interactive Food Safety Instruction Program | Utah State University will use instructional computer simulation modules to teach students about the science behind the USDA's Fight BAC! public education program, while encouraging them to adopt recommended food safety behaviors. | Ongoing. Mendenhall, Utah State University. |
| USDA | Survey and education on detection and health hazards of unapproved antibiotic residues in imported seafoods | Based on research component (see Action item #50) training materials will be developed for presentations at workshops, seminars. Research data will be disseminated through brochures, extension meetings, and professional meetings. | Ongoing. An, USC School of Pharmacy, CA<br>Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | Food Safety Education for the Hard-to-Reach and Underserved Communities | Alabama A & M University researchers will plan and implement a comprehensive, interactive food safety education program for small fruit and vegetable growers, reducing the potential for foodborne illness in hard-to-reach and underserved rural communities in Alabama and Tennessee." | Ongoing. Chemezi, Alabama A & M University.<br>Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | Food Safety Practices and HACCP (Hazard Analysis and Critical Control Point) Implementation in Assisted Living for the Elderly | S. Iowa State University will assess food safety practices and HACCP implementation in assisted living programs for the elderly. | Ongoing. Site visits completed. Gilmore, S., Iowa State University. Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | Food Safety Education for the Prevention of Foodborne Illness Among U.S. Residents 65 and Older | Kansas State University will assess food handling practices and develop a food safety education program for high-risk older adults. | Ongoing. Gordon, Telephone survey complete.<br>Kansas State University.<br>Funded through CSREES, National Integrated Food Safety Initiative 111 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Food Safety Education in the 21st Century: Improving the Process | North Dakota State University will conduct research on reducing the risk of foodborne illness outbreaks among high-risk audiences through existing public education programs Ongoing. Garden-Robinson, Training done. Analysis on focus group studies is being done. , North Dakota State University.<br>Funded through CSREES, National Integrated Food Safety Initiative 111 | Ongoing. |
| USDA | Integrated Approach to Identification of Problem Food Safety Behaviors and Customized Educational Delivery for Improving Them: A Tri-State Project for South Carolina, Georgia and North Carolina | Clemson University researchers will identify unsafe food safety behaviors and develop educational programs addressing those behaviors for non-English speaking groups and hard to reach audiences. | Ongoing. Funded through CSREES, National Integrated Food Safety Initiative 111 |
| **Action Item #46: Educate the Public About the Merits and Safety of Irradiation as One Tool To Reduce Bacterial Contamination of Food.** | | | |
| CDC | Food Irradiation Education | CDC has produced a FAQ document on the promising benefits of food irradiation. Designed to education the public and discredit any myths about the process. | Available at: http://www.cdc.gov/ncidod/dbmd/diseaseinfo/foodirradiation.htm |
| **Action Item #47: Support Community-Based Programs That Promote and Facilitate Availability of Recommended Vaccinations for Adults and Children.** | | | |
| CDC | Healthy Pets Healthy People | CDC has created this Web site to provide you with information about the health-related risks of owning and caring for animals and about the benefits of vaccinating household pets. | Available at: http://www.cdc.gov/healthypets/ |
| CDC | National Immunization Program (NIP) | NIP's mission is to reduce disease and disability from diseases that can be prevented through immunization. | Numerous ongoing projects support state and community-based programs that promote vaccination and provide vaccines. |
| CMS | CMS's National Influenza and Pneumococcal Campaign | Mission is to improve the rates of immunization among the over 65 population. Along with separate QIO efforts CMS has been building state level coalitions with CDC, carriers, intermediaries, grantees, health departments and other interested parties. The Oklahoma Foundation for Medical Quality (OFMQ) supports CMS's national campaign supports this initiative by providing technical assistance using effective systems change approaches and by developing and implementing strategies to support systems changes to pooromote flu and pneumococcal immunizations. (See www.MedQic.org) In 2004-2005 CMS will continue to evaluate environmental factors affecting the supply and demand for flu vaccines. | Ongoing effort. |
| CMS | Reduction of Healthcare Disparities Initiative | There are 52 QIO projects focused on underserved populations and the elimination of healthcare disparities, including increasing pneumonia and influenza vaccinations in this population. | Ongoing effort and is in the current QIO scope of work. Numerous ongoing projects to support community based programs that promote adult vaccinations. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| VA | 2003-2004 Influenza Pneumococcal Vaccine Toolkits | Sent to all VA healthcare facilities. | Ongoing. |
| **Action Item #48: Identify Vaccines Useful in Preventing Drug-Resistant Infections and Reducing Antimicrobial Drug Use and Evaluate Novel Methods For Improving Coverage with These Vaccines.** | | | |
| CDC | Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP) | A 7-valent conjugate vaccine for *Streptococcus pneumoniae* , licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Four CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in nine Emerging Infections Program areas in which population-based active surveillance is conducted. Second, ongoing active surveillance in these areas will track any change in the amount of invasive disease due to drug resistant strains. The third project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The fourth is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees. | Ongoing. During 2000 and 2001 the case control study protocol was developed, a pilot study was launched, and procedures manuals and tracking system were revised in preparation for the main study. During 2002, cases and controls were enrolled and main data collection began. In 2003, we completed enrollment for children <2 years and are finishing enrollment of children 2-4 years in 2004. Preliminary analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. ABCs surveillance indicates that by 2003 disease due to penicllin-resistant strains had dropped by over half. (Whitney CG, et al. N Engl J Med 2003 May 1;348(18):1737-46). In Anchorage, 4 consecutive carriage studies have been completed. While analysis is ongoing, preliminary results suggest that carriage of strains resistant to trimethoprim/sulfamethoxazole has become less common while carriage of penicillin resistant strains has not changed. |
| FDA | *H. influenzae* type B (HIB) vaccine | Monitoring of polysaccharide conjugated vaccines, including regular inspections of the production facilities, review and conduct of Lot Release studies, and review of amendments to the current Biologic License Application | Ongoing. Several licensed vaccines. Continued vaccine supply essential to maintaining the near elimination of resistant *H. influenzae* disease in the U.S. |
| FDA | Pneumococcal vaccine | Monitoring and guidance provided to current manufacturer of a seven-valent conjugate vaccine. Ongoing. One licensed conjugate vaccine for the prevention of invasive disease and acute otitis media in infants and small children. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants. One licensed multivalent polysaccharide vaccine for the elderly. | Ongoing. One licensed polysaccharide and one licensed conjugate vaccine for the prevention of invasive disease and acute otitis media. Studies suggest decrease in AR among *S. pneumonia* isolates coincident with wide spread use of conjugate vaccine in infants. One licensed multivalent polysaccharide vaccine for the elderly. |
| FDA | Pneumococcal conjugate vaccine | Identify mechanisms for establishing efficacy of additional pneumococcal conjugate vaccines with additional serotypes. Participated in multiple WHO Workshop held to discuss serologic correlates of protection. Also, provide regulatory review, conduct research and provide guidance to support licensure of additional pneumococcal vaccines (various products under IND). | Research regarding serologic assessment of response to vaccines ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Influenza vaccine | Regulatory and research support of annual trivalent inactivated and live intranasal influenza vaccine development, production and licensure, including additional manufacturers and novel technologies. | Ongoing regulatory review, research support and guidance for both current vaccines and those vaccines under IND, including vaccines against avian influenza. |
| FDA | Pertussis Vaccine | Regulatory and research support for expanding the use of pertussis vaccine into additional age groups (ie: adolescent/adult use and possibly neonatal use). | Ongoing: Participated in First International Neonatal Vaccination Workshop in March 2004. Also, participating in collaborative study with FDA, CDC and Vanderbilt University to establish a serologic diagnostic cut-off point for pertussis infection in adolescent/adults (NHNES study). |
| VA | Improve use of vaccines related to prudent use of antibiotics | Department of Veterans Affairs, Veterans Health Administration Directive 2001-053. Influenza Vaccine – Recommendations for 2001-2002. Published and placed on VA Intranet website August 28, 2001.<br>Infomercials were aired on VA Knowledge Network regarding influenza vaccine.<br>Performance Measurement Program, 2001 and 2002 VHA Performance Measurement System Technical Manuals list Influenza Immunization and Pneumococcal Immunization as Preventive Care Quality Performance Measures, with specific recommendations for these immunizations for Nursing Home Care Units within the VHA system. Influenza Vaccine - Recommendations for 2002-2003, Veterans Health Administration Directive 2002-044, Published on 7/29/02.<br>Domestic Hot Water Temperature Limits, Veterans Health Administration Directive 2002-073. | The VHA is already in the forefront of immunization practices as is evidenced by the pneumococcal and influenza vaccine usage rates compared to the national averages. In addition, influenza vaccine use increases each year in the VHA as emphasis on this program continues. Therefore, this action item is already under way and will continue to be an area of emphasis area for the VA. |
| **Action Item #49: Evaluate the Nature and Magnitude of the Impact of Using Various Antimicrobial Drugs as Growth Promotants in Different Species, Using Current Animal Husbandry Practices. Use This Information To Assist in Risk-Benefit Assessments of Such Use.** | | | |
| CDC | See Action Item #50 (Reducing resistant bacteria in food animals). | See Action Item #50 (Reducing Resistant Bacteria in Food Animals). | See Action Item #50 (Reducing Resistant Bacteria in Food Animals). |
| **Action Item #50: Conduct Additional Research To Further Define the Effects Of Using Various Veterinary Drugs on the Emergence of Resistant Bacteria That Infect or Colonize Food Animals of Different Species, Using Various Animal Husbandry Practices. Identify Risk Factors and Preventive Measures to Humans.** | | | |
| CDC, FDA | Reducing resistant bacteria in food animals | Projects assess the impact of antibiotic use in swine and cattle, develop alternatives to the use of antimicrobial drugs as growth promotants, and evaluate new practices to reduce resistant bacteria in food animals. | Ongoing. Awarded cooperative agreements to four schools of veterinary medicine (two for studies in dairy cattle, two in swine). Dairy projects have completed 5 years of research and some publications. Swine projects are completing 3rd year of work. |
| USDA | Antimicrobial Drug Use and Veterinary Costs in US Livestock Production | Report issued by ERS that evaluated the risks/benefits of antimicrobial drug use in livestock production. | Released May 2001. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | See Action Item #55 (Comparison of antimicrobial resistance in Salmonella, *E. coli* , and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia) | See Action Item #55 (Comparison of antimicrobial resistance in Salmonella, *E. coli* , and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia) | See Action Item #55 (Comparison of antimicrobial resistance in Salmonella, *E. coli* , and Campylobacter isolated from swine farms using different antibiotic regimens, in collaboration with University of Georgia) |
| **Action Item #51: Conduct Epidemiologic And Laboratory Studies To Assess the Risk of Development and Transfer of Resistance Related to The Use of Antimicrobial Drugs in Food and Non-Food Plants, and Identify Risk Factors and Potential Preventive Measures.** | | | |
| CDC | Antibiotics used as pesticides in orchards | Apple and pear orchard farmers have used streptomycin to control the plant disease fireblight, a bacterial infection caused by Erwinia amylovora, since the 1950s. After years of streptomycin use, streptomycin-resistant strains of *E. amylovora* developed. Farmers now use oxytetracycline in *E. amylovora* resistant areas to control fireblight. In this pilot study involving 4 orchards in 3 states, fruit is tested to determine whether human pathogens, including antimicrobial-resistant organisms, are present in orchards and whether antibiotic residues are potentially reaching the food supply. | Completed specimen collection; testing and data analysis in progress. Currently performing additional testing to determine antibiotic resistance in enterococci and other bacteria found in the collected specimens |
| CDC | See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations). | See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations). | See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations). |
| CDC | See Action Item #55 (Sampling for Antibiotics in agricultural river basin). | See Action Item #55 (Sampling for Antibiotics in agricultural river basin). | See Action Item #55 (Sampling for Antibiotics in agricultural river basin). |
| CDC | See Action Item #55 (Evaluation of the impact of flooding on water quality and human health indicators). | See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators). | See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators). |
| USDA | Impact of intertwined turkey-hog production on the species, strains, and antibiotic resistance of Campylobacter in turkeys | This study will investigate the potential for transfer of Campylobacter, including antibiotic resistant strains, between hogs and turkeys, raised in close proximity. This will include farms with differing uses (or non use) of fluoroquinolones. | Ongoing. Kathariou, N.C. State University<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Ecological fitness of antibiotic resistant Campylobacter in poultry | This epidemiologic and microbiological study will evaluate the spread and persistence of Fluoroquinolone-resistant Campylobacter in poultry. The information will help in the design and implementation of management measures to control the spread of resistant Campylobacter pathogens on farms and in processing plants | Ongoing. Zhang, Iowa State University<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | AR of enteric bacteria in poultry or food-producing animals | The project plan has three broad objectives: 1) determine the impact of antimicrobial use on the prevalence of drug-resistance in enteric bacteria; 2) elucidate mechanisms that contribute to the acquisition, dissemination, and persistence of antimicrobial resistance in food-borne pathogens; and 3) develop models to measure the frequency of emergence and transfer of AR. | Ongoing. Bischoff, et al, College Station, TX. |
| USDA | Sources and risk factors for Campylobacter in poultry and impact of human disease in a closed system (Iceland) | This study will look at 3 potential sources of Campylobacter and measure the risk factors for contamination of broiler flocks in a closed production system. | Ongoing. Stern, Lowman, Hiett, Athens, GA. Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Ecology of intermittent Salmonella infections in dairy milk shed | The goal is to determine the spatial and temporal attributes of the Salmonella by serotype and molecular types in dairy milk shed; compare on-farm attributes of herds; and determine intervention strategies | Ongoing. Sischo, Analysis being done. Preliminary studies show that transient birds (crows, pigeons) may play a role in between herd or between population movement of S.newport. MDR *S.newport* has adapted to a variety of ecological niches. University of California. Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | AR of foodborne pathogens linked to a multiple AR operon | This project will determine the impact of induction of *E. coli* O157:H7 and *S. Enteritidis* multiple antibiotic resistance (mar) locus on resistance to structurally unrelated compounds including antibiotics, sanitizers, and food preservatives. " | Ongoing. Have developed a real time PCR protocol for determining the expression of key genes involved in intrinsic resistance. Mathews, Rutgers University. Funded through CSREES, National Research Initiative 32.0 Ensuring Food Safety |
| USDA | Plasmid Biology 2002 Symposium | The objectives of the Plasmid Biology 2002 Symposium were to bring together scientists working in all the areas of basic and applied plasmid biology to discuss the latest progress and advances in the field. | Complete. Symposium held June 20-22, 2002. Khan, Sobecky, University of Pittsburgh. |
| USDA | Oxytetracycline resistant gram-negative bacteria in dairy cattle: risk factors and implications on food safety | The purpose of this study is to gather relevant and accurate information on the epidemiology (descriptive and molecular) of oxytetracycline resistant gram-negative bacteria in dairy cattle. This study will provide much needed scientific information with reference to prevalence, and on trends of antimicrobial resistance on the farm with respect to oxytetracycline and other antimicrobial agents. The investigators will also identify risk factors for resistance development and develop and implement interventions to reduce risk for resistance. | Ongoing. Jayarao, Preliminary data shows time withdrawal of oxytetracycline does not decrease numbers of oxytetracycline resistant bacteria. Penn State University Funded through CSREES, National Research Initiative 32.0 Ensuring Food Safety |
| USDA | Assessment of the pathogenicity of *Campylobacter jejuni* in broilers | University of Arizona researchers will determine the prevalence of the bacteria named Campylobacter jejuni in broiler chickens. This bacteria is a source of foodborne illness in humans. The grant will also be used to train processors to identify those broiler chickens that may have the bacteria. | Ongoing. Joens, Sampling completed. University of Arizona. Funded through CSREES, National Integrated Food Safety Initiative 111 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Interventions for controlling AR of Salmonella and Campylobacter in dairy cattle | Michigan State University will develop methods to control microbes in dairy cattle from becoming resistant to the antibiotics that kill foodborne pathogens | Finished. Kaneene, Michigan State University. Banked isolates of Salmonella and *C. jejuni* are available for further research. Some descriptive data available regarding the differences of antibiotic resistance prevalence in organic versus traditional farms. Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Source, diversity and resistance of foodborne pathogens in swine and pork | North Carolina State University researchers will investigate the source, diversity and resistance of two harmful bacteria (Salmonella, campylobacter and Yersinia) in two sets of swine: one that has received antibiotics and one that is free of antibiotics. The investigation will help predict which group of swine will be more resistant to the pathogens and less expensive to own. | Ongoing. Gebreyes, North Carolina State University. Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | The moral economy of antimicrobials in animal agriculture: advancing policy and practice in an era of AR | Texas A&M University researchers will identify optimum approaches for managing and regulating antimicrobial use while developing and delivering a curricula and educational materials on antimicrobial resistance for use by veterinarians and cattle producers. | Ongoing. Scott, Texas A&M University Funded through CSREES, National Integrated Food Safety Initiative 111 |
| **Action Item #52: Develop Rapid Tests For Inspecting Fresh Commodities Like Fruit For Evidence Of Contamination With Bacteria That Are Resistant To Antibiotics.** | | | |
| FDA | Rapid methods development | Validated culture methods for the identification of foodborne pathogens in animal feed. Contaminated animal feed may be a source of human foodborne pathogens, and resistant foodborne pathogens, for animals. For example, Salmonella and other enteric organisms can be spread by rodents, flies, birds, etc, and animal feces may also contaminate the feed. Validated cultural methods for foodborne pathogens will be compared to rapid test methods for foodborne pathogens-rapid methods will later be optimized. | Extramural contract with University of Tennessee awarded. |
| **Action Item #53: Evaluate the Effect of Current Food Processing and Distribution Methods on the Emergence and Spread of Drug-Resistant Organisms.** | | | |
| FDA | NARMS retail food | Monitor prevalence of antimicrobial resistant zoonotic pathogens among foods of animal origin. | NARMS retail was initiated in 2002 and now includes 10 of the 11 FoodNet sites. |
| **Action Item #54: Identify and Evaluate New Food Pasteurization Strategies.** | | | |
| **Action Item #55: Assess the Risk of AR Emergence and Spread due to Environmental Contamination by Antimicrobial Drugs or by Resistant Bacteria in Animal and Human Waste. Collect Information on Whether Environmental Contamination by Antimicrobial Drugs Can Lead to the Development of Resistance in Bacteria That Live in Soil or Water.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations | Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment. | Enzo R. Campagnolo, et. al. Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations. The Science of The Total Environment, Volume 299, Issues 1-3, Pages 89-95, November 2002. |
| CDC | Sampling for antibiotics in an agricultural river basin | Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities. | Report of preliminary findings is currently being reviewed and edited. More refined analysis of results for journal publication is in progress. |
| CDC | Evaluation of the impact of flooding on water quality and human health indicators | Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water. | Preliminary results presented at CDC CAFO workshop, Feb 2004. Some analysis still pending. |
| FDA | Animal production studies | Determine dynamics of resistance development in naïve animal populations exposed to antimicrobial agents. | Completed animal studies focusing on the development and persistence of bacteria resistant to fluoroquinolones and streptogramins. |
| USDA | Enteric pathogens in oysters | This study will assess the relationship between fecal coliforms present in the water column and the prevalence of pathogens in oysters sold in retail markets. It will try to determine primary sources (human vs. agricultural) of fecal contamination, | Ongoing. Joens, University of Arizona.<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Presence and fate of antibiotics and hormones in mushroom farming | The mushroom industry uses large volumes of poultry and horse manure to prepare the compost for mushroom growing. This project will examine the fate of common antibiotic and hormone compounds in compost and mushroom samples. | Ongoing. Suri. Villanova University.<br>Funded through CSREES, National Research Initiative 32.0 Ensuring Food Safety |
| **Action Item #56: Assess the Impact of Antimicrobial Use in Companion Animals (Pets) on Colonization and Infection with Drug-Resistant Organisms in The Animals and Their Humans Household Contacts.** | | | |
| **Action Item #57: Work with Veterinary and Agricultural Communities To Help Educate Users of Veterinary and Agriculture Antimicrobials About AR Issues, and Promote the Implementation and Evaluation of Guidelines That Address These Issues.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC, FDA, USDA | Liaison with American Veterinary Medical Association Steering Committee on Antimicrobial Resistance | Participate in committee activities, including development of prescribing principles and educational programs. | The committee developed General Principles for Judicious Therapeutic Use of Antimicrobial (1998), which were then adapted by species groups for their membership, to date including swine (1999), poultry (2000), bovine (2000), feline (2001), and equine (2001). Implementation is promoted through educational programs and a computerized veterinary decision support system, which is under development. |
| USDA/FDA | Education programs to producers | University based programs to educate producers on the difference between A.R. and residues. | Ongoing |
| CDC | Development of model veterinary school curriculum to promote appropriate antimicrobial drug use . | A curriculum is being developed in collaboration with partners that will be offered to veterinary schools. Completed curriculum will consist of Background Module and several Species Specific Modules (dairy cattle, small animal, poultry, etc.). | Ongoing. Continuing development of Web-based course material with partners at Michigan State University, College of Veterinary Medicine. Nearing completion of draft Background Module. |
| FDA | Education/outreach materials | Develop outreach material on judicious use targeted to veterinarians. | Ongoing activity. Contract awarded with the American Veterinary Medical Association to develop the guidelines. Guidelines received and from these, videotapes and brochures produced for veterinary practitioners.<br>1) Published four booklets that explain prudent use principles in depth for beef, dairy, swine and poultry veterinarians and sent the appropriate booklet to food animal practitioners.<br>2) Produced two videotapes to be used at meetings and veterinary medical schools to introduce the prudent drug use principles. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **** TOP PRIORITY ****<br>**Action Item #58: In Consultation with Stakeholders, Refine and Implement the Proposed FDA Framework for Approving New Antimicrobial Drugs for Use in Food-Animal Production and, When Appropriate, for Re-Evaluating Currently Approved Veterinary Antimicrobial Drugs.** | | | |
| FDA | Drug categorization | Develop an approach for how to evaluate drugs as to their importance in human medicine for use in animal drug premarket application requirements for use in CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern. | Ongoing. An approach for ranking antimicrobial drugs as to their importance for human medicine was developed by CDER and incorporated into CVM's draft guidance published in November 2002. Comments on the approach were obtained from the CDER Anti-infective Advisory Committee in January 2003 and incorporated into the final guidance that published in October 2003. |
| FDA | Fluoroquinolones | Withdraw approval of fluoroquinolones for use in poultry | Sarafloxacin voluntarily withdrawn April 30, 2001; hearing requested for Bayer's enrofloxacin. Legal proceedings ongoing. Both sides have filed narrative statements, written direct testimonies, and detailed proposed findings of fact. Oral cross examination took place between April 28 and May 9, 2003. Final briefs and reply briefs were filed in July and August, 2003. On March 16, 2004, Administrative Law Judge Daniel Davidson issued an initial decision, ordering the approval of the NADA for that drug for use in poultry be withdrawn, effective on the date the initial decision becomes final. Pursuant to 21 CFR 12.120(e) this initial decision will become the final decision of the Commissioner by operation of law in the absence of the timely filing of exceptions under 21 CFR 12.125(a) or the filing of a notice pursuant to 21 CFR 12.125(f) that the Commissioner intends to review the decision. |
| FDA | Risk assessment | Risk assessment: Conduct an analysis of the relationship between emergence of streptogramin-resistant *Enterococcus faecium* (Synercid) in humans and use of streptogramins (virginiamycin) in food-producing animals. | Draft risk assessment for distribution and public comment planned for 2004. |
| FDA | Pathogen load | Develop guidance relating to antimicrobial drug effects on pathogen load and incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern. | Literature review published on CVM website May 2001. Veterinary Medicine Advisory Committee meeting held January 22-24, 2002. Based on the lack of scientific consensus on the issue, CVM has decided not to pursue guidance regarding pathogen load effects at this time. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Microbiological safety requirements | Develop pre-approval requirements for microbiologic safety regarding the use of antimicrobial agents in food-producing animals. Incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiologic effects on bacteria of human health concern. | Draft guidance for industry was published in September 2002. Public meeting was held in October 2002 to present guidance document and obtain public comment. Comment period from the guidance closed in November 2002 and an analysis of comments received has been completed. Final guidance was published in October 2003. |
| FDA | Antimicrobial use in food-producing animals | Develop rulemaking relating to annual reports of use and quantity of antimicrobial drugs marketed for food animals | Participated in WHO expert consultation on monitoring drug use in September 2001. Developed draft proposed rule and guidance. FDA is holding proposed rule and guidance while assessing economic impact of the proposed regulation. |
| FDA | Framework document | Refine the Framework Document and incorporate the concepts into guidance for industry on a strategy for assuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern. | Comments from public meetings and submitted to the Framework Document have been incorporated into guidance; small, outreach meetings held with stakeholder groups throughout 2001 for additional input. Key concepts from the Framework Document have been incorporated into the draft guidance for industry published in November 2002. Final guidance was published in October 2003. |
| **Action Item #59: Strongly Encourage Involvement of Veterinarians in Decisions Regarding the Use of Systemic Antimicrobial Drugs in Animals, Regardless of the Distribution System Through Which the Drug Is Obtained (e.g., Regardless of Whether a Prescription Is Required To Obtain the Drug).** | | | |
| FDA | Educational materials | Develop outreach materials on judicious use targeted to food animal producers. | Based on the information developed for veterinarians, FDA developed and printed booklets for swine producers and poultry producers, written with less technical language. Have contracted with specialists to write booklets for dairy and beef producers. These booklets have been printed and distributed. |
| FDA | AR use by veterinarians | Develop a Web-based decision support system for use by veterinarians to select and use antimicrobial agents appropriately. | Provided funding for development of Veterinary Antimicrobial Decision Support System; five year contract awarded late 2001. |
| **Action Item #60: Evaluate the Potential Impact of Making All Systemic Veterinary Antimicrobial Drugs Available by Prescription Only.** | | | |
| **Action Item #61: Convene an Expert Group To Consider How To Incorporate AR Issues into Regulations Governing the Registration and Use of Antimicrobials and Antibiotic Pesticides. Invite External Experts, Stakeholders, and the Public To Provide Input.** | | | |
| **Action Item #62: Establish an Ongoing Mechanism To Obtain Periodic Input from External Experts on AR Issues. This Process Will Include Ensuring Input from Stakeholders and Partners (e.g., State and Local Health Agencies, the Private Sector, and the Public) in Developing and Reviewing Federal Efforts To Address Antimicrobial Resistance.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| ARHQ, CDC, DoD, VA, EPA, FDA, NIH, USDA | Antibiotic resistance task force | Annual Progress Report and Public Meeting. | In 2003, progress report issued consisting of inventory of projects that address Action Plan items. Third annual public meeting June 30, 2004, Bethesda, MD. Convened consultants meeting to discuss issues relating to writing of Part II of the Action Plan (Global Issues), September 26, 2002, San Diego, CA. Sent Task Force Representative to World Health Organization to help WHO implement Global strategy on AR. |
| CDC | Board of Scientific Counselors, National Center for Infectious Diseases | Discussion of CDC activities to address AR at Board meetings, including extended discussion in breakout group in 2002. | Ongoing. |
| **** TOP PRIORITY ****<br>**Action Item #63: Support Demonstration Projects To Evaluate Comprehensive Strategies That Use Multiple Interventions To Promote Appropriate Drug Use and Reduce Infection Rates.** | | | |
| CDC | Wisconsin Antibiotic Resistance Network (WARN) | The Wisconsin Antibiotic Resistance Network (WARN) is a statewide program to reduce antibiotic overuse and reduce the spread of resistant bacteria that cause upper respiratory illnesses. WARN is a partnership between the State Medical Society of Wisconsin, the Marshfield Medical Research Foundation, and the Wisconsin Division of Public Health. Activities include antimicrobial susceptibility testing; implementation and evaluation of educational interventions for the community, health departments, and health professionals, pharmacy outreach, and economic analyses to determine intervention costs. | Ongoing. A plan for the transition from the CDC Cooperative Agreement to a statewide coalition was devised and steps were implemented throughout 2003. In addition, the WARN program continued activities intended to raise awareness and knowledge among consumers and providers about appropriate antibiotic use. These activities resulted in over 35 educational seminars presented to child care professionals and parents, the development and dissemination of a CD-ROM, and informational mailings to over 55,000 providers and consumers.<br>During 2003 surveillance for drug-resistance S. pneumoniae infections through the Wisconsin Department of Health continued as well as the analyses of prescribing trends/data from healthcare data. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | The Chicago Antimicrobial Resistance Program (CARP) | CARP is a 5-year demonstration program to determine the impact of antimicrobial use and infection control interventions on the reduction of antimicrobial resistance in a healthcare delivery system. Components include developing improved methodology for interhospital and intrahospital comparisons of AR rates, computer-based surveillance of antimicrobial drug use, and interventions to improve antimicrobial drug use and prevent emerging resistance. The program has demonstrated methods for adherence to hand hygiene, decreases in rates of MRSA and VRE, reductions in use of broad-spectrum antibiotics and antimicrobial regimens with redundant antimicrobial spectra, and model the costs of healthcare associated infections. | Ongoing. Supported by CDC Cooperative Agreement through 2003. 2003 accomplishments include measured increases in adherence to hand hygiene practices, measured increases in compliance with guidelines for treating infections, decreases in inappropriate use of antimicrobials, and an overall decrease in MRSA and VRE . Implemented electronic surveillance for identification of new antimicrobial starts for patients in long-term healthcare and developed web-based program to access patients' new antimicrobial starts and associated pharmacy, laboratory, and demographic data. |
| CDC | IMPART (Inter-Mountain Project on Antimicrobial Resistance and Therapy) | A project to implement and evaluate a comprehensive approach in rural Utah and Idaho communities (in both inpatient and outpatient settings) for surveillance of AR, to improve antimicrobial prescribing, to assess the environmental impact of antimicrobial drug use in agriculture and aquaculture and to evaluate potential routes of transmission of resistant bacteria to humans, and to identify novel biotherapeutic approaches to AR that have applicability to the rural setting. | Three year grant awarded in 2001. During the first year of this study a comprehensive surveillance system has been established to monitor AR and assess the impact of antimicrobial drug use in agriculture and aquaculture. Data collection is underway with preliminary results expected in 2003.<br>Pillai SK, et al.,. Prevalence of the fsr locus in Enterococcus faecalis infections. J Clin Microbiol. 2002; 40(7):2651-2652<br>Satish K. Pillai et al., Effects of glucose on Enterococcus faecalis biofilm regulation by the quorum-sensing fsr locus. 2004; J Infect Dis. Accepted for publication |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities | This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System (TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies. | Ongoing. Initiated pilot testing of the interventions in two hospitals within the network (University of Pittsburgh Medical Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital) during 2001. Follow-up observations show significant improvement in compliance across all occupations. Problems hindering compliance which continue to be targeted include unreliable delivery of isolation materials, inconsistent identification of patients requiring isolation, and time consuming inefficiencies in the delivery of patient care services such as medication administration. In addition, an assessment of policy, perception, and practice regarding MRSA control has been initiated. In 2003 we conducted a survey of knowledge, attitudes, and practices in facilities, and evaluated TPS in an inpatient surgical unit at PRHI which measured a decline of 54% in healthcare associated - MRSA infections. |
| VA | See Action Item #39. | See Action Item #39. | See Action Item #39 |
| **Action Item #64: Utilize Federal Health Care Systems (e.g., DoD, VA) as Models for AR Surveillance and Prevention and Control Activities Involving Appropriate Drug Use, Optimized Diagnostic Testing, Infection Control, and Vaccination Practice.** | | | |
| VA | See Action Item #39. | See Action Item #39. | See Action Item #39. |
| **Action Item #65: For All Healthcare Systems for Which Federal Funds Are Provided, Identify and Promote Strategies To Establish AR Prevention and Control Activities as Part of Quality Monitoring Programs.** | | | |
| VA | Quality assurance programs | The Office of Quality and Performance's Performance Measurement Program, which supports the VHA Strategic Plan, serves as a vehicle for effecting change in a balanced fashion. The Performance Plan operationalizes the premise that better quality, access, and satisfaction are often more efficient. For example, improved rates of inexpensive pneumococcal vaccinations may result in decreased antibiotic use. Immunization rates are assessed through a contract chart review system and are part of managers' performance standards, and, therefore, are used as part of the VHA quality-monitoring program. Excellent immunization rates in the VHA have resulted from this program. JCAHO Safety Goal #7 - Hand Hygiene to reduce healthcare-associated infections were addressed in a memorandum by VA Under Secretary for Health. AHRQ StudyToward a Safety Culture: Reducing Nosocomial Infections. This study seeks to translate evidence-based practices in nosocomial infection at 10 Cincinnati hospitals' ICUs and ORs to reduce infection, decrease hospital costs and improve patient outcome. | Ongoing. The VA Under Secretary for Health's hand hygiene memorandum was issued to VA medical facilities nationwide on 12/15/03. The study "Toward a Safety Culture" is in process. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **Action Item #66: Encourage Nationally Recognized Accrediting Agencies such as The National Committee for Quality Assurance (NCQA), and the Joint Commission on Accreditation Standards That Promote Efforts To Prevent and Control AR, Including Appropriate Use, Infection Control, Vaccine Use, and Diagnostic Testing. These Standards May Draw on the Findings of Existing Data and Demonstration Programs and AHRQ Evidence-Based Practice Centers.** | | | |
| AHRQ | Research Project (R01): National trends in outpatient quality indicators. | Using data from the National Ambulatory Medical Care Surveys and the National Hospital Ambulatory Medical Care Surveys, the investigator will construct and apply a set of outpatient quality indicators, including antimicrobial use (e.g., in viral respiratory infections). | Study currently in progress. |
| **Focus Area III: Research** | | | |
| **Action Item #67: Additional Research, Including High Risk and High Payoff Research in Nontraditional Fields, Is Needed.** | | | |
| CDC | Grant Program for Applied Research on Antimicrobial Resistance: Microbiologic Mechanisms of Dissemination of AR Genes and Relationship to Antimicrobial Drug Use | Awards for projects to develop information necessary to prevent and control the emergence and spread of resistance in selected bacteria through better understanding the mechanisms through which resistance develops and spreads in field settings. | Three year awards were made in 2001. Research areas included AR among *E. faecium* in animal and human populations and fluoroquinolone resistance among *E. coli* in healthcare settings. Projects underway, results pending. |
| CDC | Grant Program for Applied Research on Antimicrobial Resistance: Characterization of Strains of Community-Associated Methicillin-Resistant *Staphylococcus aureus* | This research includes three components that will provide information needed to prevent and control AR: (1) Identification and access to a defined population of persons within which community- associated MRSA disease and data appear to be sufficiently prevalent to allow appropriate analyses; (2) obtaining strains of *Staphylococcus aureus* (*S. aureus*) causing disease in this population with appropriate, linked epidemiologic and clinical data; and (3) characterizing MRSA strains using a variety of molecular and biochemical techniques. | Five three years awards were made in 2003. Recipients are Harbor-University of California Los Angeles Research & Education Institute, University of California – San Francisco, University of Chicago, and William Beaumont Hospital. " |
| CDC | AR mechanisms of *S. pneumoniae (*Alaska) | Use of PCR methodologies to rapidly screen *S. pneumoniae* isolates for genetic determinants of resistance; monitoring the emergence, spread, persistence, and decline of multidrug-resistance organisms by molecular-based typing capabilities to include multilocus sequence typing (MLST). | Ongoing. In 2002, expanded surveillance methodologies to include the molecular typing techniques Pulse Field Gel Electrophoresis (PFGE) and Multi Locus Sequence Typing (MLST) which allow an enhanced understanding of the emergence and transfer of resistance genes among these Pneumococcal isolates. Began retrospectively screening previously collected multidrug resistant isolates using these molecular typing techniques. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH, DoD | Biotechnology Engagement Program (BTEP) | The BTEP Program is an attempt by the U.S. government to engage former Soviet Union scientists that conducted biowarfare research to refocus on issues of mutual benefit. DMID program staff oversee a U.S. – Russian Collaborative TB research project initiated in 2001 with Professor A. Llyichev of Vector in Novosibirsk entitled, "Drug resistant tuberculosis in Western Siberia." Staff oversee, "Molecular epidemiology and antibiotic resistance of bacterial infections in Georgia" in collaboration with Lela Bakanidze of the National Center for Disease Control of Georgia. | Ongoing. |
| FDA | Multi-drug resistant TB | Identified genetic mechanisms causing resistance in multi-drug resistant tuberculosis. | Ongoing. |
| FDA | Role(s) of mutators in natural populations | Conduct research on genetic diversity within populations of bacterial pathogens; Determine if mutator subpopulations of *Salmonella enteritidis* promote antibiotic resistance; Investigate role of bacterial persistence in emergence of AR. | Ongoing. |
| FDA | Acquisition of antibiotic resistance in Salmonella Newport | Investigate acquisition of multi-drug resistance in Salmonella Newport; Determine how resistance patterns, sources of organisms, and PFGE profiles correlate with phylogenetic distribution. | Ongoing. Completed study comparing *S. Newport* isolates of human and food animal origin with regards to antimicrobial resistance patterns, specific antimicrobial resistance genes and genetic relatedness. |
| FDA | DNA microarray profiling of antibiotic resistance genes. | Develop DNA microarray techniques and DNA chips for characterizing antibiotic resistance genes for multiple bacterial pathogens. | Ongoing. In conjunction with scientists at the University of Maryland, developed over 60 PCR primers to target genes associated with resistance in Salmonella and *E. coli* to 6 categories of antimicrobial agents, including B-lactams, aminoglycosides, phenicols, tetracyclines, and sulfonamides. |
| FDA | Antibiotic resistance in vibrio | Investigate emergence of antimicrobial resistance in Vibrio species. | Onging |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Studies on the Mechanism of fluoroquinolone (FQ) resistance and molecular screening for resistance determinants in Campylobacter, E. coli, and Salmonella | Isolate and characterize FQ resistant Campylobacter, E. coli and Salmonella from chicken and turkey farms. | 21 FQ resistant campylobacter were isolated from chicken liver samples and characterized by PCR-RFLP and Pulsed field gel electrophoresis (PFGE). Seventy-eight campylobacters were isolated from turkey litter samples and characterized for the presence of galE gene, PCR-RFLP and PFGE. Quinolone resistance determining regions (QRDR) from campylobacters and *E. coli* were PCR amplified and sequenced for the detection of silent mismatched mutations. The FQ resistant *E. coil* strains isolated from chicken and turkey litter were typed by ribotyping. Completed in vivo studies examining the development of fluoroquinolone resistance among Campylobacter from chickens administered approved fluoroquinolones. Continue to characterize at the molecular level, resistant Salmonella, Campylobacter and *E. coli* as part of the NARMS retail program. |
| FDA | Fate and degradation of antimicrobials, oxytetracycline (OTC) and sulfadimethoxine-ormetoprim (Romet 30) from aquaculture environmental samples | To isolate and characterize OTC and Romet 30 resistant Aeromonas spp., Pseudomonas, Citrobacter and *E. coli.* From aquaculture and catfish tissues. | 30 OTC resistant *Aeromonas spp* . have been isolated. These isolates have been characterized by PFGE. These investigations are still in progress. |
| FDA | Develop a microarray chip for the detection of multiple antibiotic resistance markers | Oligonucleotide probes to detect resistance markers for 17 different antibiotics would be embedded in microarray slides. These would be hybridized with in vitro-labeled cDNA of the resistant bacteria isolated from farm animals or clinical samples. The microchip would help FDA efficiently monitor and track resistant markers and make regulatory decisions. It would also aid physicians for choosing appropriate antibacterial therapy. | Ongoing. |
| FDA | Elucidation of the mechanism of resistance development in anaerobic bacteria from human intestinal tract | Evaluation of the effect of fluoroquinolones on the resistance development in the bacteria from the human intestinal tract and analysis of the fluoroquinolone resistance mechanism in anaerobic bacteria from the human intestinal tract. | Ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Biodegradation of fluoroquinolone antibiotics | The fungus Pestalotiopsis guepini metabolized the fluoroquinolone antimicrobial agent norfloxacin to 7 amino-1-ethyl-6-fluoro-4-oxo- 1,4 dihydroquinolone-3-carboxylic acid and three other metabolites during growth on rice hulls used as poultry litter, suggesting that fungi that grow on poultry litter may be able to metabolize residues of fluoroquinolone drugs. The intestinal bacterium Enterococcus durans degraded 1-phenylpiperazine to N-acetyl-1-phenylpiperazine, N-formylaminoethylaniline and 2-phenylaminoethanol, suggesting a potential role in the breakdown of other compounds, such as fluoroquinolone drugs, that contain a piperazinyl group. | Ongoing. |
| FDA | Blood borne pathogens | Develop rapid assays to identify blood borne pathogens using nucleic acid based tests (NAT) and a TaqMan assay to detect bacterial contamination in whole blood and platelets. | Ongoing research to develop a DNA microarray based pathogen chip that could detect all pathogenic bacteria that contaminate blood and blood products. |
| NIH | NIH CRISP Database | CRISP <http://crisp.cit.nih.gov/> (Computer Retrieval of Information on Scientific Projects) is a searchable database of federally funded biomedical research projects conducted at universities, hospitals, and other research institutions. The database, maintained by the Office of Extramural Research at the National Institutes of Health (NIH), includes projects funded by NIH, Substance Abuse and Mental Health Services Administration (SAMHSA), Health Resources and Services Administration (HRSA), Food and Drug Administration (FDA), Centers for Disease Control and Prevention (CDC), Agency for Healthcare Research and Quality (AHRQ), and Office of Assistant Secretary of Health (OASH). Users, including the public, can use the CRISP interface to search for scientific concepts, emerging trends and techniques, or identify specific projects and/or investigators. | Ongoing |
| NIH | Innovative approaches for combating antimicrobial resistance | This initiative is designed to stimulate novel and innovative research, including high risk and high payoff studies in nontraditional fields, to acquire a better understanding of the factors affecting the development of resistant pathogens and spread of resistance genes, in order to direct actions to diagnose, control, and treat AR. | Ongoing. RFA-02-009, Receipt date for applications 10-10-02, 98 applications received, 18 funded in early 2003. Projects include: "Using Genomics to Identify Antibiotic Sensitivity Genes," "Predicting Resistance: Validating Mathematical Models," "and "Ciprofloxacin resistance and compensatory mutations," among others. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Investigator-initiated small research grant award program announcement (R03) | The R03 award supports small research projects that can be carried out in a short period of time, with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding. | Ongoing. Program Announcement (PA-03-108) released on April 18, 2003; expiration date: April 18, 2006. Recently funded a project entitled "Novel Antibiotics: Site-Specific Recombination Inhibitor" under this PA. |
| NIH | Investigator initiated grants mechanisms (R01) | NIH funds a diverse portfolio of grants to study AR in major viral, bacterial, fungal, and parasitic pathogens. Projects include basic research into the disease-causing mechanisms of pathogens, host-pathogen interactions, and the molecular mechanisms responsible for drug resistance, as well as applied research to develop and evaluate new or improved products for disease diagnosis, intervention, and prevention. | Ongoing. Examples of recent R01 awards include: "Structure-Based Antimicrobial Design," "Molecular Targets in Peptidoglycan Synthesis," "3-Ketoacyl ACP Synthase III: A Novel Antibiotic Target," and "Biosynthesis of Beta-Lactam Antibiotics." |
| NIH | Small Business Innovation Research and Technology Transfer Research Program (SBIR/STTR) | The SBIR/STTR program is an omnibus solicitation established under federal law that seeks to use small business to stimulate technological innovation, increase the participation of small business in federal R&D, and to increase private sector commercialization of technology development through Federal R&D. The annual set-aside for agencies with extramural research budgets over $100M is 2.5%. | Ongoing. Recent awards include: "Dual Purpose b-Lactamase Inhibitors," "Developing Novel Antibiotics Against Yesinia Pestis," "Novel Agents for Antibiotic Resistant Anthrax," "Discovery of Anti-bioweapon Agents in BAC Libraries," "Broadly Active Inhibitors of High Priority Pathogens," " Potentiating Compounds for Aminoglycoside Antibiotics," "Novel Treatment for Septicemia Targets A1 ARs," and "Identification of E.coli Anti-Infective rRNA Targets." |
| NIH | Cooperative Research for the Development of Vaccines, Adjuvants, Therapeutics, Immunotherapeutics & Diagnostics for Biodefense | To support discovery/design and development of vaccines, therapeutics, adjuvants, and diagnostics for biodefense. This program will help translate research from the target identification stage through target validation to early product development. | Multiple awards made in 2003, including "Novel Antibiotics against Gram-Negative Bacteria," and "Gram-Negative Sepsis: Pharmacophore-Based Therapeutics." |
| NIH | Food and Waterborne Diseases Integrated Research Network (FWDIRN), expansion of the Enteric Pathogens Research Unit | NIAID's FWDIRN network will include multidisciplinary research on all food and waterborne pathogens (bacteria, viruses, and protozoa), as well as toxins, to facilitate the development and evaluation of products to rapidly identify, prevent, and treat food and waterborne diseases that threaten public health. The network will include Immunology (IRU), Microbiology (MRU), Zoonoses (ZRU) and Clinical (CRU) Research Units. The Network will be supported by a Coordinating and Biostatistics Center. One of the MRUs will emphasize research aimed at developing and evaluating therapies for botulism. | Five units and a Coordinating and Biostatistics Center were awarded in 2003. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Biodefense and Emerging Infectious Diseases Research Opportunities | In response to growing concerns about the use of biological agents in acts of terrorism, NIAID has expanded its biodefense research program. The ultimate goal of that expansion is to develop effective diagnostics, vaccines and therapeutics to protect the public in the event of a biological attack or the sudden emergence of select rare or eradicated diseases. | PA-03-080; http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html. Expires March 2006. Recent awards made under this initiative include: "Beta-lactamase Antibiotic Resistance of B. anthracis," and "Development of DHPS as a Bioterrorism Therapeutic Target." |
| NIH | "Immune Mechanisms in Polymicrobial Infections" Symposium | This symposium is planned for the 2004 American Society for Microbiology general meeting. The goals and objectives of this workshop are consistent with program objectives to understand host factors associated with susceptibility to infections and with the research scope and objectives of recently released RFA A1 02-008 on "Impact of Microbial Interactions on Infectious Diseases". | ASM Meeting will be held May 23-27, 2004. |
| NIH | Scientific Advance: Reemergence of Chloroquine-Sensitive Plasmodium falciparum Malaria after Cessation of Chloroquine Use In Malawi | Malawi became the first country in that continent to replace chloroquine (CQ) with fansidar as the primary treatment for malaria. The switch was made as CQ was no longer clinically effective against falciparum malaria. Using molecular techniques on stored samples, these investigators showed that the vast majority (85%) of parasites isolated from patients in 1992 contained a mutation, known as pfcrt76T, that conferred resistance to CQ when parasites were cultured in vitro. Over the time period during which CQ was not being used, the percentage of parasite isolates bearing the mutation has diminished dramatically; no pfcrt76T mutant parasites were identified in samples obtained in 2001. Importantly, the "restored" clinical efficacy of CQ was shown in a clinical trial to treat malaria in adults. These results indicate the lack of drug pressure favors the CQ sensitive parasite variants over the CQ resistant parasites. Thought will have to be given on the reintroduction of CQ, e.g. by using drug combinations, so as not to repeat past experience. | Kublin JG, Cortese JF, Njunju EM, Mukadam RAG, Wirima JJ, Kazembe PN, Djimde AA, Kouriba B, Taylor, TE and Plowe CV: Reemergence of chloroquine-sensitive Plasmodium malaria after cessation of chloroquine use in Malawi. J Inf Dis 187: 1870-1875, 2003. |
| NIH | Scientific Advance: Penicillin response genes in drug-resistant pneumococci. | Investigators have identified a new set of genes that play a critical role in the expression of penicillin resistance in pneumococci. The importance of these observations is that they offer a potential alternative target against penicillin resistant pneumococci. It is expected that specific inhibitors of the mur genes would resensitize resistant bacteria to penicillin. Several laboratories have began to search for such inhibitors. If successful, such a search would identify inhibitors that could be valuable additions to the arsenal of antimicrobial agents against drug resistant pneumococci. | Filipe SR, Severina, E, Tomasz A. The murMN operon: a functional link between antibiotic resistance and antibiotic tolerance in *Streptococcus pneumoniae* . PNAS 99: 1550-1555, 2002. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Scientific Advance: A novel class of antibacterial agents discovered | The most effective long-term solution to problems of resistance is perhaps the development of drugs that act on new targets. One such target is LpxC, which is a vital enzyme involved in the biosynthesis of lipid A, a key component of the outer membrane of Gram-negative bacteria. Investigators have recently developed a unique chemical technology that generated a significant collection of a novel family of compounds (called oxazoline hydroxamic acids) as candidate inhibitors for LpxC. This method proved to be quite reliable and resulted in the formation of very high purity compounds that could be directly used for biological testing. When tested against LpxC and *E. coli* , a number of active compounds with structures falling outside earlier-known structural classes were discovered. In addition, several important structural features that facilitate enzyme binding were observed. This knowledge may aid in the design of other novel antibacterial agents. | Pirrung MC, Tumey LN, McClerren AL, and Raetz CR: High-Throughput Catch-and-Release Synthesis of Oxazoline Hydroxamates. Structure–Activity Relationships in Novel Inhibitors of E. coli LpxC: In Vitro Enzyme Inhibition and Antibacterial Properties. J. Am. Chem. Soc. 125:1575-1586, 2003. |
| USDA | Poultry: A food animal model for following antimicrobial resistant Enterococci | There is continued concern about the use of antibiotics as growth promoting agents in food animals and the potential for development of AR in human pathogens. The long term goal of this study is to understand the processes involved in the development and spread of resistance in gram positive bacterial flora of poultry. This study will collect microflora samples from commercial poultry farms and processing/slaughter plants for one year. The farms will have one house using growth promoting antibiotics throughout the flocks' life and one house with no antibiotics used. Comparisons of drug resistance genes and plasmids will be made between poultry gram-positive commensals and human enterococci. The human samples will be obtained from NARMS. | Ongoing. Hofacare, University of Georgia<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Prevalence, strain types and antibiotic resistance of Campylobacter in turkey grow-out farms | Campylobacter is a leading cause of human food-borne illness in the U.S. Transmission involved primarily poultry, although pork, beef, raw milk, and other sources have also been identified. Resistance to several antibiotics, including fluoroquinolones, commonly used for treatment of human infections, is increasing in Campylobacter. Extensive studies with broilers suggest that birds become colonized in the farm, usually without symptoms, and that meat becomes contaminated during slaughter and processing. This study will investigate the prevalence of Campylobacter in sixty turkey growout farms in Eastern North Carolina. It will evaluate the impact of distinct turkey husbandry practices in the grow-out turkey farms, and of antibiotic use for veterinary purposes, on Campylobacter prevalence, strain types, and AR profiles. The results from this study will provide a currently unavailable database on Campylobacter colonization, subtypes and AR in turkeys. | Ongoing. Kathariou. North Carolina State University Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Clonal dissemination of antimicrobial resistant *Campylobacter jejuni* and *Escherichia coli* | There is an increasing concern that AR in both pathogenic bacteria and in the normal flora present a risk to the public health, and reduction in the degree of AR is an important public health goal. The antibiotic resistant flora that appear after antibiotic exposure of cattle and other food animals may be 'new' antibiotic resistant strains originating on the farm, or may be pre-adapted strains that originated elsewhere and were transferred to the farm by animals, feed, water, wildlife, humans, or other mechanisms. The origin is important, since different origins require different control measures. For *Salmonella typhimurium*, wide dissemination of AR strains is the predominant process. This study will look at whether wide dissemination of antibiotic resistant strains is also important in *Campylobacter jejuni* and *E.coli* in the bovine intestine. In addition, this study will determine whether AR *E.coli* can be competitively displaced by non- antibiotic resistant strains. | Ongoing. Besser, Washington State University Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Determinants of AR in *Escherichia coli* isolated from calves | The goals of this project are to describe the dynamics of antibiotic resistance in commensal *Escherichia coli* isolated from calves, link the patterns of resistance to management and environmental attributes, define the economics of antibiotic use, and develop educational modules to describe approaches that minimize the occurrence of AR bacteria. | Ongoing: Sischo, University of California, Vet Med Teaching and Research Center. Funded through CSREES, National Integrated Food Safety Initiative 111 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Antibiotic usage and risk factors for AR in pork production | This three year study is designed to determine an association between the use of antimicrobial agents in swine production and the presence of AR in human foodborne pathogens isolated from slaughter pigs. | Ongoing: Norby, Large Animal Clinical Sciences, Michigan State University.<br>Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | Antimicrobial drug use and the development of resistant Enteric bacteria in dairy cattle | The objectives of this study are to 1) Determine the effect of antimicrobial treatment on the development of resistance in bacteria present in dairy cattle, 2) Develop and apply prudent antimicrobial-use guidelines specific for dairy cattle, and 3) Disseminate these guidelines to dairy producers and their veterinarians. It is expected that scientifically based interventions will be obtained and disseminated for use by veterinarians and dairy producers to address important issues of public health concern which pose a threat to their future livelihood. | Ongoing: Wittum, The Ohio State University<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Factors affecting the emergence of quinolone-resistant Campylobacter in poultry | The main goal of this project is to use an integrated approach to study quinolone-resistant campylobacters in the poultry reservoir and to establish an education and extension program on AR. | Ongoing: Zhang, Food Animal Health Research Program, The Ohio State University<br>Funded through CSREES, National Research Initiative 32.1 Epidemiological Approaches to Food Safety |
| USDA | Determination of the relationships between antibiotic resistance and virulence in Salmonella | Bacterial strains were obtained from clinical cases of salmonellosis and ARS found that a small group of multiple antimicrobial resistant Salmonella are capable of secreting a cytotoxin. The results demonstrate that the hypervirulent abilities of multiple AR Salmonella could be due to an ability to damage cells within a host. | Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center (NADC). |
| USDA | Develop a fundamental understanding of the process of antimicrobial resistance in order to prevent the spread of unwanted resistant factors among the microorganisms that live normally in the gut of swine and cattle | ARS used continuous culture models of gut bacteria to determine the effect of the drug vancomycin on bacteria within the continuous culture model and within the gut of animals. Although ARS previously demonstrated that growth of certain vancomycin-resistant microorganisms was prevented in the model by the bacterial mixture, ARS found that a sub-therapeutic concentration of vancomycin in the growth media will allow these microorganisms to survive in the culture. This information will be used to determine antimicrobial dose and duration regimens that are therapeutically effective but limit the spread of antibiotic resistant bacteria, and will ultimately lead to more appropriate approaches to using antibiotics in food animal agriculture. | Ongoing: USDA-ARS: College Station, TX. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Determination of the persistence of antimicrobial resistant pathogens in the environment | The persistence of AR bacteria following the cessation of use of a given antibiotic is a problem for the development of effective intervention strategies to combat antimicrobial resistance. In collaboration with the FDA Center for Veterinary Medicine, ARS examined the antimicrobial resistance patterns of disease causing strains of *Escherichia coli* from newborn pigs experiencing diarrhea. ARS found that 53% of the isolates were resistant to chloramphenicol, a broad spectrum antibiotic that has been banned for use in food animals in the United States since the mid 1980s. This information will help to determine the factors that govern the persistence of resistance genes once an antibiotic is no longer used in animal agriculture. | Ongoing: USDA-ARS College Station, TX. |
| USDA | Assessment of the effect of penta-resistant bacteria on virulence and/or colonization | ARS challenged broiler chicks on the day of hatch with either a sensitive or penta-resistant Salmonella typhimurium DT104 and determined that penta-resistant bacteria did not cause clinical illness in broiler chicks. However, ARS did observe a significant increase in the numbers of birds that were colonized in the penta-resistant group. In contrast to in vitro studies, these data indicate that acquisition of multiple resistance does affect colonization rates but may affect the numbers of bacteria that may reach the food chain. | Ongoing: USDA-ARS: Athens, GA. |
| USDA | Characterization of Salmonella serotypes on their ability to cause disease in animals and to acquire and disseminate AR genes | We determined that Salmonella serotypes differ in their ability to persist within the host and environment and have determined that both integrons (mobile genetic elements) and plasmids, play a role in dissemination of resistance genes. | Ongoing. USDA/ARS Athens GA |
| USDA | Characterization of 3rd generation cephalosporin resistant Salmonella from animal sources | We characterized the strains and resistance mechanisms of 3rd generation cephalosporin resistant Salmonella in the United states and found that the CMY-2 gene is the most common mechanism by which Salmonellas acquire this resistance in the US. | Ongoing. USDA/ARS Athens GA |
| USDA | Characterization of erythromycin resistance in enterococci isolated from swine farms using different regimens of tylosin | The effect of tylosin use on erythromycin resistant enterococci isolated from farms was investigated. Results from the study suggested that although resistance was higher on a farm where tylosin was used as a growth promotant, a few resistant enterococci also persisted on a farm where no antimicrobials were being used. Isolates from farms were analyzed for antimicrobial resistance gene content as well as genetic determinants for dissemination of resistance. | Ongoing. USDA/ARS Athens GA |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Evaluation of prevalence and antimicrobial susceptibility of *E. coli* isolated from fruits and vegetables | In collaboration with scientists from USDA-AMS, we are evaluating the prevalence and antimicrobial susceptibility of generic *E. coli* isolated from fruits and vegetables collected from different regions of the US. This information will be useful for determining the effect of antimicrobials on *E. coli* isolated from these sources and the potential impact that these bacteria may have on consumer health. | Ongoing. USDA/ARS Athens GA |
| USDA | Evaluate the effect of Ionophores on fecal shedding of pathogens | We examined the effects of three ionophores (monensin, laidlomycin propionate, and bambermycin) on *Escherichia coli* O157:H7 and *Salmonella typhimurium* in experimentally infected sheep. Ionophore treatment had no significant effect on fecal shedding of the pathogens, on occurrence of the pathogens in lumen contents, nor on antimicrobial susceptibilities of the recovered isolates. The results suggest that short-term feeding of ionophores would have little or no adverse effect on Salmonella and *E. coli* populations in the ruminant. | Ongoing. Southern Plains Agric. Research Center, College Station TX" |
| USDA | Evaluate the effects of low level feeding of antibiotics on microbial diversity and inhibitory stringency | We used a defined mixed culture of chicken gastrointestinal microflora maintained in a continuous-flow chemostat as a model to study the effects of the antibiotic tylosin on microbial diversity and inhibitory stringency. The microbial diversity in cultures treated with sub-therapeutic concentrations of tylosin was reduced (from 29 initial organisms to 3 after treatment), and the treated cultures failed to exclude *E. coli* O157:H7 in vitro. These results suggest that the use of tylosin at low doses for growth promotion may eliminate some beneficial anaerobic bacteria that normally serve as a natural host defense against enteric infection. Further research in a live animal model is warranted to determine whether tylosin treatment increases susceptibility of chickens to colonization by enteric pathogens. | Ongoing. Southern Plains Agric. Research Center, College Station, TX." |
| USDA | Elucidate genetic mechanisms contributing to the acquisition, dissemination, and persistence of antimicrobial-resistance in food-borne pathogens | A gene cluster encoding high level macrolide antibiotic resistance was found in a strain of *Aeromonas hydrophila* , a Gram-negative fish pathogen and opportunistic human pathogen, that had been isolated from a diarrheic pig. This gene cluster was located adjacent to a class 1 integron present on a promiscuous Tn21-like transposon demonstrating a conjugation frequency of 3.5 × 10-3. Additional studies are underway to determine if the practice of feeding fish meal to swine contributes to the carriage of pathogenic aeromonads in swine. | Ongoing. Food and Feed Safety Research Unit, ARS College Station, TX. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Factors affecting vancomycin-resistant Enterococcal infections | Human vancomycin-resistant Enterococcus (VRE) infections may increase in humans following prophylactic and therapeutic treatment with vancomycin, while VRE colonization in poultry may increase following consumption of vancomycin-like antibiotics fed as additives to improve performance. Results from studies with broilers have indicated a need for a healthy digestive microflora capable of preventing the increased gut colonization by VRE that may occur following administration of vancomycin-like drugs. In cooperation with a human infectious disease medical specialist, we have developed a competitive exclusion culture against VRE infection for prophylactic and therapeutic applications in hospital settings. More recent research revealed that an obligatory and least cost effective infusion of anaerobic gases into the culture is not needed for the successful maintenance of an anaerobic atmosphere and the culture. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Investigating potential links between decreased susceptibility to disinfectants and resistance to antibiotics | There is evidence that the use of biocides may contribute to the development of antibiotic resistance. A study of 89 b-hemolytic *Escherichia coli* isolated from neonatal swine with diarrhea revealed that of those *E. coli* isolates exhibiting reduced susceptibility to the commonly used biocide chlorhexidine, most clustered in one ribogroup, most were resistant to six antibiotics and that the decreased susceptibility was correlated with four virulence factor genotypes, STA, STB, SLT2, and F107 (# 1). The correlation of chlorhexidine resistance to ribogroups and to the presence of virulence factors suggests that the use of disinfectants may select for enterotoxigenic strains of *E. coli* in certain animal production settings. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Characterization of disturbances and alterations in the microbial ecology of continuous-flow culture models of the gastrointestinal tract | A mixed continuous flow culture of anaerobic microflora from the gastrointestinal tract of chickens is being used to determine whether probiotic cultures are more efficacious if the constituents are niche adapted to one another. This culture is also used to evaluate the effect of antibiotics, with varying activities, on the efficacy of CE cultures and provides a model in which the host's immune response is not a factor. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Establish a model for quantitative determination of rates of antimicrobial resistance acquisition | The objective of the study was to determine the frequency of spontaneous acquisition of resistance to select antibiotics by *Salmonella typhimurium* when grown in pure culture in a glucose limited continuous flow culture at slow (D= 0.025 h-1) or fast (D=0.27 h-1) dilution rates. Results suggest that spontaneous acquisition of resistance to the select antibiotics was highly unlikely regardless of growth rate or exposure to lethal or sublethal antibiotic concentrations. Future studies are underway to expand the model to a mixed microbial ecosystem containing transmissible genetic elements. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Investigate the effect of ionophore feeding (long-term) on pathogen populations and antimicrobial susceptibility in stocker cattle | A collaborative project with the USDA-ARS Dale Bumpers Small Farm Research Center is being conducted determine the effect of long-term ionophore feeding on pathogen populations and antimicrobial susceptibility in stocker cattle. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Surveillance of antibiotic resistance in normal enteric bacteria | The project goal is to determine if the commensal bacterium, *Megasphaera elsdenii* , can be a useful indicator species of antibiotic resistance status in livestock since it is indicative of the normal gut microbiota. A survey was conducted of the antibiotic resistance found in *M. elsdenii* , when isolated from livestock species with different environmental conditions and feeding regimes. Current results indicate that bacteria from feral swine that are not exposed to modern antibiotics have very low levels of tetracycline resistance compared to those strains isolated from both organic and conventionally raised swine. | Ongoing. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa. |
| USDA | Exploring opportunities for technology transfer to the field of human medicine | The project goal is to determine if *M. elsdenii* is a normal bacterial inhabitant of the human GI tract and if this bacterium can be used as an indicator of enteric species in humans for antibiotic resistance status. | Ongoing. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Normal enteric bacteria as a reservoir for antibiotic resistance | The project goal is to determine if nonpathogenic commensal bacteria and protozoa in the gut can be a reservoir for antibiotic resistance genes and if these genes can be transfered to other bacterial pathogens. This work includes: a. Megasphaera elsdenii and its resistance to tetracyclines have been chosen as a model system for investigation. A survey of M. elsdenii and resistance status in swine, cattle, sheep and goats is currently underway. b. Antibiotic resistance is linked to bacterial survival within enteric protozoa of the rumen. Protozoa can facilitate antibiotic resistance gene exchange and bacterial survival in adverse environments. The project goal is to determine if rumen protozoa can harbor resistant bacteria within intracellular vacuoles and if vacuoles can stimulate gene transfer between resistant and susceptible bacteria. We have observed that only Salmonella strains which possess the DT104 gene cluster for antibiotic resistance survive protozoal exposure and were hyperinvasive and more virulent. Precise mechanisms that link virulence, survival and resistance are und | Ongoing. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa |
| USDA | Identification of oligopeptide inhibitors of antibiotic resistance | Certain oligopeptides can inhibit the production of specific proteins responsible for antibiotic resistance in Salmonella, Shigella and *E coli* . The project goal is to determine the range and diversity of these inhibitory peptides and determine their mode of molecular action. Additional targets of inhibition are being sought in larger scale synthesis and screening projects. | Ongoing. Preharvest Food Safety and Enteric Diseases, ARS, Ames, Iowa. |
| USDA | Characterize Salmonella serotypes for their ability to cause disease in animals and to acquire and disseminate antimicrobial resistance genes | Although there are over 2,400 different serotypes of Salmonella, they differ in their ability to cause disease in humans and animals, acquire resistant attributes, and colonize and persist with the host and environment. Salmonella serotypes were first characterized by their antimicrobial resistant pattern followed by molecular characterization in which mechanisms of resistance and genetic relatedness among other isolates of the same serotype were determined. Collaborations on these endeavors took place between scientists within the AARU and scientists in other ARS research units. These data demonstrated that Salmonella serotypes differ in their ability to persist within the host and environment and have determined that both integrons (mobile genetic elements) and plasmids play a role in dissemination of resistance genes. The data are being used by scientists studying the epidemiology and pathogenesis of salmonella. | Completed - Antimicrobial Resistance Research Unit, ARS, Athens GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Characterize 3rd generation cephalosporin resistant Salmonella from animal sources | We characterized the strains and resistance mechanisms of 3rd generation cephalosporin resistant Salmonella in the United states and found that the CMY-2 gene is the most common mechanism by which Salmonellas acquire this resistance in the US. This is in contrast to Europe where it is the Extended Spectrum Beta-Lactamase (ESBL). We found that isolates carrying the CMY-2 gene are significantly more likely to have multiple drug resistance, and that certain Salmonella serotypes were more likely to carry the resistance. Third generation cephalosporins are important antimicrobials used to treat severe infections in both humans and animals. The research resulted in a predictive diagnostic test for multiple drug resistant Salmonella. Turkeys, horses, cats and dogs aresignificantly more likely to have these isolates than cattle, swine, chicken and exotics. The multiple drug resistance identified was found to be encoded on a large transferable plasmid, and this information will be used by scientists studying resistance mechanisms and veterinarians and physicians who routinely use cephalosporins in treatment. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA. |
| USDA | Determine the effect of different antimicrobial use regimens in swine production on the development and maintenance of resistance among Salmonella, Campylobacter, Enterococci and *E. coli* | The epidemiology of Salmonella, Campylobacter, Enterococci and *E. coli* on swine farms using three different antimicrobial regimens was assessed. Results indicated that more resistance was identified in bacteria isolated from the farm using antimicrobials both sub-therapeutically and therapeutically. However, resistant bacteria were found to persist on the farm that has not used antimicrobials for the past 30 years. | On-going. Antimicrobial Resistance Research Unit, ARS, Athens GA. |
| USDA | Characterize mechanisms of resistance to extended spectrum b-lactams in Salmonella from animal sources | Recently, the numbers of Salmonella isolates resistant to the third generation cephalosporins have increased. To investigate the increase in resistance, a diverse group of Salmonella serotypes resistant to ceftiofur was selected. Those strains were analyzed for the presence of the CMY-2 AmpC type b-lactamase gene. The majority of strains contained the CMY-2 gene. Most of the strains also contained large plasmids and are being subjected to Southern analysis to determine the location of the CMY-2 gene. The strains were also analyzed for the presence of the integron 1 gene, intI1. Most strains positive for intI1 were Salmonella serotype Newport, Heidelberg, or Typhimurium. | On-going. Antimicrobial Resistance Research Unit, ARS, Athens GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Determine the effect of antimicrobial selective pressure on the rate of spread of *Salmonella typhimurium* in poultry | Salmonella strains have arisen that are resistant to multiple antimicrobials including 3rd generation cephalosporins. The ability of those strains to be transmitted between hosts and under antimicrobial selective pressure is presently unknown. Two Salmonella strains (one pan-susceptible and one resistant to 12 antimicrobials used in the NARMS program) were compared by a natural transmission study in chickens in the presence of MIC levels of chlortetracycline (tet). The percentage of positive cloacal swabs from birds exposed to the resistant strain indicated that more birds were positive when tet treatment was administered. Cloacal swabs from the susceptible strain exposed birds indicated that more birds were positive in the absence of tet treatment. The same results were observed for tissues at necropsy on D10. Results indicated that resistant strain did not transmit faster in the presence of tet, and suggested that use of tet had a protective effect on tissue colonization. | On-going, Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Develop an assay for the detection of horizontally acquired antimicrobial resistance genes in Salmonella and other bacteria | Previously, PCR techniques and Southern analysis have been used to identify specific resistance genes. In order to increase the speed, efficiency, and sensitivity and to broaden the applicability of these techniques, a DNA microarray to perform multiple simultaneous assays for a broad range of antimicrobial resistance genes is being designed to incorporate current PCR product probes as well as synthetic oligonucleotides. These microarrays will be able to assay the antimicrobial resistance gene content of any number of diverse bacterial species, especially those under NARMS surveillance. This information can be used by other scientists when they study mechanisms of resistance among bacterial species. | On-going. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | To phenotypically and genotypically characterize Salmonella serotype Newport identified from NARMS 2000 and 2001 collection of isolates | Between 2000 and 2001, the animal arm of NARMS recovered a total of 241 Salmonella newport non-diagnostic (slaughter and on-farm) isolates. MDR S. newport isolates were recovered more frequently than pan-susceptible isolates and most of the MDR isolates were resistant to > nine antimicrobials. None of the Newport isolates contained Class 2, Class 3, or Class 4 integrons (intI2, intI3, or int4, respectively). However, Class I (intI1) integrons were identified in most of the animal species regardless of whether they were MDR or pan-susceptible. Large and small plasmids were identified mainly in the MDR Newport isolates. By PFGE analysis, Newport appears to be heterogeneous among multiple animal species, but homogeneous in a particular species. These data can be used for comparison with isolates obtained from human outbreaks to determine if a particular animal species served as the source of infection. The molecular mechanisms of resistance can be evaluated in order to determine the cause of dissemination of the serotype and the increase in antimicrobial resistance within the serotype. | On-going. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Assess the occurrence of Salmonella serotype Typhimurium DT104 in retail ground beef | Salmonella was isolated from 3.5% of samples and eight serotypes were identified including Typhimurium. Phage typing indicated that they were DT104A, a subtype of DT104. Generic E. coli was also isolated from 25% of samples. Comparison of antimicrobial resistant profiles between Salmonella and *E. coli* did not indicate that genes were being transferred among isolates. These data indicate that DT104A can be isolated from ground beef but the significance is unknown. Further, these multi-resistant *E. coli* are infrequently found in ground beef. This information can be used by other scientists and the beef industry for designing and implementing reduction and control programs. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA. |
| USDA | Evaluate the prevalence and antimicrobial susceptibility of *E. coli* isolated from fruits and vegetables | Although a number of studies have determined levels of resistant bacteria on meat items from grocery stores, few studies have been conducted on the prevalence of bacteria from fruits and vegetables. In collaboration with scientists from USDA-AMS, we evaluated the prevalence and antimicrobial susceptibility of generic *E. coli* isolated from fruits and vegetables collected from different regions of the US and determined that resistance to 17 different antimicrobials among these *E. coli* is low. | This information will be useful for determining the effect of antimicrobials on *E. coli* isolated from these sources and for studying the potential impact that these bacteria may have on consumer health. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Determine the presence of *E. coli* 0157:H7 in swine | Data indicated that is was possible to isolate *E. coli* 0157:H7 from the colons of pigs presented at slaughter, although the recovery rate was low. Even though the recovery rate was low, the presence of 0157:H7 may have a significant impact on human health if contaminated meat is handled or consumed. Further studies are required to determine the true prevalence and risk of *E. coli* 0157:H7 in swine. This information can be used by other scientists and the swine industry for designing and implementing reduction and control programs. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA and ERRC, Wyndmoor PA. |
| USDA | Assess the prevalence of *E. coli* 0157:H7 in downer cows | As a team member, the laboratory participated in a study to assess the prevalence of *E. coli* 0157:H7 in downer cows. Data indicated that 4.9% of downer cows versus 1.5% of health cows harbor *E. coli* 0157:H7 in their colons. Not all isolates were clonal, resistance to antimicrobials was low and very little multiple resistance was observed. These data implicate downer cows as having a higher prevalence of *E. coli* 0157:H7 than healthy cows and may affect the use of downer cows as sources of meat. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA and ERRC, Wyndmoor PA. |
| USDA | Determine the effect of three feed-based antimicrobials (apramycin, carbadox, and tetracycline) on the development of antimicrobial resistance in generic *E. coli* | Resistance to tetracycline in *E. coli* varied widely by sample, group, and trial. However, a significant increase in the percentage of resistant isolates was observed in piglets fed antimicrobials when compared to controls. Resistance to apramycin also increased in piglets when compared to controls. However, upon removal of apramycin, resistance in *E. coli* declined. Resistance to carbadox remained unchanged after feeding carbadox when compared to controls. Piglets fed low doses of antimicrobials demonstrated improved growth when compared to controls. These data are useful for veterinarians, pharmaceutical manufacturers, and scientists as they devise ways to limit the development of resistance to antimicrobials while maintaining animal health. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA. |
| USDA | Characterize antimicrobial resistance, species, and genetic diversity of Campylobacter isolated from feedlot cattle | In collaboration with scientists from USDA-APHIS-VS-CEAH, antimicrobial resistance was examined in Campylobacter isolates from feedlot cattle as part of a NAHMS study. Results indicate that a majority of the isolates were susceptible to the antimicrobials that were tested and that there is significant genetic diversity among isolates. These data provided a significant overview of antibiotic resistance among Campylobacter from healthy beef cattle across the US. This work will be useful to beef producers, regulatory agencies and researchers in antimicrobial resistance. | Ongoing. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | To increase recovery of Campylobacter from various sources | Because of the fastidious nature of Campylobacter, recovery from meat or other sources is difficult. We developed an enhanced methods for recovering Campylobacter from chicken carcass rinsates by employing a centrifugation step of the rinsate prior to enrichment in culture media. This resulted in a >50% increase in the recovery of Campylobacter. This is significant in that previous methods were leading to the isolation and under reporting of Campylobacter in samples. This work will be useful to scientists involved in Campylobacter research. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Determine the prevalence and level of Campylobacter in parents (breeders) and offspring (broilers) of commercially reared pigs | Studies were conducted to determine the prevalence and level of Campylobacter in parents (breeders) and offspring (broilers) of commercially reared pigs | Prevalence of Campylobacter ranged from 42 to 100% positive in three broiler offspring flocks (90% of breeders were shedding). This research will assist in the development of effective intervention strategies to reduce Campylobacter in poultry and will be useful to scientists involved in Campylobacter research. |
| USDA | To evaluate the prevalence and antimicrobial resistance of enterococci isolated from retail food items | In a study of retail food (meat, vegetables, and fruit) collected from grocery stores in NE Georgia, enterococci were isolated, identified to species, and tested for antimicrobial susceptibility. Results indicated that although enterococci were prevalent among food items, resistance to antimicrobials used in human medicine was very low (linezolid, gentamicin, ciprofloxacin) or nonexistent (vancomycin). This was the first study analyzing enterococci isolated not only from meats, but fruits and vegetables as well. This work will be useful to scientists involved in Enterococcus research as well as regulatory agencies and the industry as they develop and implement mitigation strategies. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Characterize erythromycin resistance in enterococci isolated from swine farms using different regimens of tylosin | The effect of tylosin use on erythromycin resistant enterococci isolated from farms was investigated. Results from the study suggested that although resistance was higher on a farm where tylosin was used as a growth promotant, a few resistant enterococci also persisted on a farm where no antimicrobials were being used. Isolates from farms were analyzed for antimicrobial resistance gene content as well as genetic determinants for dissemination of resistance. These data provide insight as to the development and persistence of resistance on-farm and will be useful to research and industry scientists as they develop and implement Enterococcus mitigation strategies. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Characterize aminoglycoside resistance among enterococci isolated from poultry | Aminoglycoside antimicrobials are of interest due to their use in both animals and humans. In this study, resistance to aminoglycosides in enterococci from poultry samples was examined. High-level gentamicin, kanamycin, and streptomycin resistance was found in 23%, 41%, and 19% of the isolates, respectively. Of the ten aminoglycoside resistance genes examined, five were identified in the isolates using PCR. Seven resistant *E. faecalis* isolates were negative for all genes tested suggesting that additional resistance genes may exist. Phylogenetic analysis revealed that the isolates were genetically different with little clonality. Data from this study suggest that enterococci from poultry are diverse and contain potentially unidentified aminoglycoside resistance genes. This work will be useful to scientists involved in Enterococcus research as well as the industry as they develop and implement mitigation strategies. | On-going. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Evaluate the effect of media, temperature, and culture conditions on the species population and antimicrobial resistance of enterococci | Although optimal growth conditions for enterococci are well-established, a paucity of information exists on the influences of growth conditions on the overall population or antimicrobial resistance of enterococci. In this study, the effect of temperature, culture media and enrichment period was examined. Data indicated that increased temperature favored the selection of E. faecium and E. hirae, while lower temperature (37oC) favored growth of *E. faecalis* , *E. casseliflavus* , and *E. durans* . In addition, significantly lower numbers of *E. faecalis* were isolated from Enterococcosel agar while higher numbers of E. faecium were isolated from Enterococcosel agar. For antimicrobial resistance, significant differences were found in the number of ciprofloxacin, linezolid or nitrofurantoin resistant *E. faecalis* and linezolid or Synercid resistant *E. faecium* due to media. Temperature influenced the number of bacitracin, flavomycin, gentamicin, nitrofurantoin, penicillin, streptomycin or tetracycline resistant *E. faecalis* and gentamicin, kanamycin, penicillin, streptomycin, | Completed. Antimicrobial Resistance Research Unit, ARS, Athens GA. |
| **Action Item #68: Conduct Further Government-Wide Assessments with External Input on the Scope and Composition of AR Research To Identify Research Opportunities.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Antimicrobial strategies and cardiothoracic surgery working group | Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery, including complications relating to the development of AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures. | Meeting held April 4-5, 2002 in Bethesda, MD., collaborative clinical trials and research initiatives under development. |
| NIH | Prevention and Treatment of *Staphylococcus aureus* Infections after Cardiac Surgery Request for Information | A Request for Information was released on October 15, 2003 to obtain information from the academic and industrial communities as to the availability and current development status of immunologic products to prevent and treat *S. aureus* infections. | Information was received from over 20 academic and industrial groups indicating the availability and current status of their products to prevent and treat *S.aureus* infections. |
| NIH | "Prevention and Treatment of *Staphylococcus aureus* Infections after Cardiac Surgery" Request for Proposals | NHLBI is taking the lead on developing a request for proposals for two parallel clinical trials to prevent and treat infections after cardiac surgery. | Ongoing discussions to determine the optimal clinical design and cost for two parallel trials to prevent and treat infections after cardiac surgery. |
| **Action Item #69: Work with the Appropriate Peer Review Structures To Ensure That the Requisite Expertise Is Applied to the Review Process To Facilitate Funding of Quality AR Research.** | | | |
| NIH | Bacteriology and mycology study sections | Recommendations for additional scientific reviewers with expertise in AR be added to selected study sections. | Recommendations were made, and selected reviewers with expertise in AR were added to study sections. |
| NIH | The Panel on Scientific Boundaries for Review has conducted a comprehensive examination of the organization and function of the review process that is carried out by the Center for Scientific Review (CSR) at NIH. The purpose of this evaluation is to position the CSR peer review system so that it fosters expanded research opportunities, as well as permits the review system to keep pace with the accelerating rate of change in the way that health-related research is performed. This examination is being carried out in two phases, with extensive involvement of the extramural research community. The Panel has proposed a set of Integrated Review Groups (clusters of scientifically related study sections, referred to as IRGs) and proposed guidelines for study sections. | The Infectious Diseases and Microbiology IRG review by the Expert Working Group was conducted from May – August 2001 and developed a proposed set of guidelines and shared interests for new study sections. NIH's CSR has established a new Study Section, Drug Discovery and Mechanisms of Antimicrobial Resistance (DDR), within the new Infectious Diseases and Microbiology Integrated Review Group (IRG). It will review applications that are concerned with the identification of novel antimicrobial agents, including agents that could be used in bioterrorism, for the prevention and treatment of infectious diseases and the study of the evolution, mechanisms, and transmission of resistance. | NIH's CSR has established a new Study Section, Drug Discovery and Mechanisms of Antimicrobial Resistance (DDR), within the new Infectious Diseases and Microbiology Integrated Review Group (IRG). It will review applications that are concerned with the identification of novel antimicrobial agents, including agents tht could be used in bioterrorism, for the prevention and treatment of infectious diseases and the study of the evolution , mechanisms, and transmission of resistance. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| **** TOP PRIORITY ****<br>**Action Item #70: Provide To the Research Community Genomics and Other Powerful Technologies To Identify Targets in Critical Areas for the Development of New Rapid Diagnostics Methodologies, Novel Therapeutics, and Interventions To Prevent the Emergence and Spread of Resistant Pathogens. Examples Include Tools Such as Microbial Genome Sequences, Information on Comparative Genomics, DNA Chip Technology, Informatics, and Assistance in the Application and Use of These Tools.** | | | |
| NIH, USDA, FDA, EPA, FDA | Microbe project interagency working group | NIAID staff is participating in the Microbe Project Interagency Working Group, which developed a coordinated, interagency five year action plan on microbial genomics, including functional genomics and bioinformatics in 2001 . | In 2002, this working group has continued to coordinate genomic activities across federal agencies including those related to biodefense and has also focused on issues related to genomic data release and usage and genomic databases; (http://www.ostp.gov/html/microbial/start.htm). |
| FDA | Genomics and Proteomics | Research in support of the use of genomics, proteomics and other powerful technologies to identify targets in critical areas for the development of new rapid diagnostic methodologies, novel therapeutics, and interventions to prevent the emergence and spread of resistant pathogens. | Established microarray group and CBER core program (for producing and reading oligonucleotide microarray chips). Initiated several research projects related to vaccine development, AR, pathogen identification and detection. Developed a rapid typing method for Neisseria gonorrhoeae applicable to non-cultured specimens and the identification of ciprofloxacin resistant strains. Also developing rapid DNA assays to detect all four species of human malaria parasites. |
| NIH | The tuberculosis research materials and vaccine testing contract (Colorado State University) | Through this contract, NIAID provides TB research reagents to qualified investigators throughout the world, enabling them to work with consistent, high quality reagents prepared from the highly contagious and technically demanding TB causative pathogen. Starting in 2002, this contract calls for making reagents available for functional analysis of mycobacteria. Screening potential TB vaccine candidates in appropriate animal models is also conducted through this contract. | During 2003, 121 individual vaccines or adjuvant candidates have been tested under this contract with 15 vaccine testing experiments completed, 16 experiments in process and seven under development. New Service: DNA-based TB microarrays are now available for qualified applicants. Information, reagent request forms, and microarray applications are available at: http://www.cvmbs.colostate.edu/microbiology/tb/top.htm. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | NIAID pathogen functional genomics resource center (PFGRC) | The PFGRC was established by The Institute for Genomic Research, on behalf of the NIAID, to provide the research community with a centralized resource to aid functional genomics research on human pathogens and invertebrate vectors of infectious diseases. The PFGRC provides scientists with free of charge genomic resources and reagents such as microarrays, protein expression clones, genotyping resources, and bioinformatics services. The PFGRC also supports the training of scientists in the latest techniques in functional genomics and emerging genomics technologies. For more information about the PFGRC please see: www.niaid.nih.gov/dmid/genomes/pfgrc/default.htm | Ongoing. |
| NIH | Sequencing of whole pathogen genomes | NIAID has made significant investment in large-scale projects to sequence the genomes of medically significant bacterial, fungal, and parasitic pathogens. In addition, NIAID collaborates with other funding agencies to sequence larger genomes of protozoan pathogens such as the organism that causes malaria. A listing of currently active pathogen genome sequencing projects is available at http://www.niaid.nih.gov/cgishl/genome/genome.cfm. The availability of microbial and human DNA sequences will open up new opportunities and allow scientists to examine functional analysis of genes and proteins in whole genomes and cells, as well as the host immune response and an individuals' genetic susceptibility to pathogens. | As of FY2003, NIAID has supported approximately 42 large scale DNA sequencing genome projects for microbial pathogens and invertebrate vectors of infectious diseases, including new projects for Burkholderia thailandensis, different strains and clinical isolates of *Bacillus anthracis* and another strain of *Clostridium perfringens.* Genome sequencing projects for bacteria *Bacillus anthracis* , *Bacillus cereus* , *Burkholderia mallei* , *Clostridium perfringens* , *Escherichia coli* (K1 RS218), *Streptococcus agalactiae* , *Rickettsia rickettsi* i, *Rickettsia typhi, Salmonella typhi,* and Wolbachia were completed. In addition, DNA sequencing projects have been completed for parasites Leishmania major, *Trypanosoma cruzi* , and *Cryptosporidium parvum* (bovine isolate). In total, NIAID-investigators have completed genome sequencing projects for 37 bacteria, 5 parasitic protozoa, and 1 invertebrate vector of infectious disease. |
| NIH | NIAID pathogen genomics website: www.niaid.nih.gov/dmid/genomes/ | The updated NIAID genomics website serves as a focal point to disseminate to the scientific community current information about NIAID's microbial genomics research program and related activities, including information on funding opportunities, policies, application procedures, priorities for large-scale genome sequencing projects, press releases, and currently funded large-scale genome sequencing projects. | Currently available to the scientific community. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Sexually transmitted pathogen genomic resources | NIAID continues to provide support for databases of genomic and postgenomic information on sexually transmitted pathogens; http://www.stdgen.lanl.gov/ | Currently available to the scientific community. |
| NIH | Bioengineering Consortium (BECON) | BECON is a trans-NIH committee composed of representatives from each of the NIH centers, institutes and divisions, including representatives from other federal agencies www.grants.nih.gov/grants/becon/becon.htm. | In FY2003, NIAID continued to participate in two BECON program announcements that support multi-disciplinary research with a focus on bioengineering to develop knowledge and/or methods to prevent, detect, diagnose or treat disease or to understand human health and behavior. These grants allow biomedical research scientists to partner with scientists from other disciplines including physics, mathematics, chemistry, computer sciences, and engineering to approach current complex biological problems. |
| NIH | Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) contract | The network includes approximately 73 registered users including basic researchers, clinical laboratories and infectious disease clinicians involved in staphylococcal AR research. NARSA supports electronic sharing of information, a yearly investigator's meeting, and a case registry and repository of well-characterized staphylococcal isolates including the newly emerged vancomycin resistant *Staphylococcus aureus* isolates. | The repository now includes a representative panel of clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from a variety of disease conditions, research isolates, genome sequenced isolates, virulence and toxin-producing strains, and a broader representation of drug-resistant strains. NARSA has also sponsored a staphylococcal annotation meeting in collaboration with the Institute for Genomic Research (TIGR) and a community MRSA meeting in collaboration with CDC. Plasmid sequence and annotation of the Michigan VRSA is now available through the TIGR CMR site on the NARSA homepage. Information concerning NARSA can be found at: www.narsa.net. |
| NIH | Respiratory Pathogens Reference Laboratory Support Request for Proposals | NIAID awarded a contract to the University of Alabama (Moon Nahm, PI) for a Respiratory Pathogens Reference Laboratory [RFP DMID 03-37]. This contract will provide a resource facility with a major effort on reagent and assay development for measurement of the human immune response to targeted bacterial respiratory pathogens that include Streptococcus pneumoniae, group A streptococci, group B streptococci, *Hemophilus influenzae* b, nontypable *H. influenzae*, *Chlamydia pneumoniae*, *Mycoplamsa pneumonia*, *Neisseria meningitides*, and *Moraxella cattaralis*. Support is included for the distribution of procedures and reagents, as well as training. | Ongoing. Current emphasis is on the development of standardized pneumococcal functional assays and advanced serotyping methodology. |
| NIH | Brochure on NIAID's microbial genomics research program | This brochure highlights recent accomplishments in the areas of genome sequencing of microbial pathogens and invertebrate vectors of infectious disease as well as related functional genomic activities. | Ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Research Center Grant, "Structural Organization and Proteomics of TB" | Under this award (P50GM62410), a global consortium consisting of over 130 laboratories from 65 institutions in 14 countries are determining and analyzing the structures of over 400 functionally relevant *M. tuberculosis* proteins. | To date, the consortium has crystallized 70 proteins and solved 27 structures (models built). The structural and functional information is publicly available through web-based databases: http://www.doe-mbi.ucla.edu/TB/. |
| NIH | Structural Genomics of Pathogenic Protozoa | NIAID has cofunded the Structural Genomics of Pathogenic Protozoa (http://depts.washington.edu/sgpp/) to provide the three dimensional structure of many proteins deduced from the genome information of the trypanosomatid and Plasmodium species. This will be valuable information for future drug and vaccine discovery design, as well as information for the discovery of new protein folds and function. | Ongoing. |
| NIH | Malaria Research and Reference Reagent Resource (MR4) Center | The MR4 continues to provide expanded access to quality controlled reagents for the international malaria research community. The website averages more than 3,000 visitors per month, and acquires and distributes more than 150 items per month to researchers worldwide. The MR4 has compiled a Laboratory handbook on "Methods in Malaria Research", available as a resource to scientists. In addition, to facilitate training and field application of new scientific methods, the MR4 provided material support for a workshop on "Microarray Technology for Malaria Parasites" (Thailand, March 2003), and has continued to distribute and support the development of new resources, including new microarrays and databases for genomic analysis of the parasite and vector. | Ongoing. |
| NIH | Application of Exploratory/Developmental Technologies to NIAID-funded Research | Program announcement (PAS-02-160) that solicited R21 grant applications as supplements to ongoing/active NIAID grants. The goal was to facilitate the application of innovative/emerging technologies to currently funded research projects related to the study of infectious diseases, diseases caused by category A agents of bioterrorism, HIV/AIDS, basic immunology, and immune mediated conditions. The program was designed to allow funded investigators to capitalize on scientific opportunities that would augment the value of the project and might not have been available at the time of submission. | In 2002, 84 grant applications were received and 28 funded. NIAID has recently re-released this PA for 2003. http://grants2.nih.gov/grants/guide/pa-files/PAS-02-160.html |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | NIAID Microbial Sequencing Centers | The Microbial Genome Sequencing Centers (MGSCs) address NIAID's need for sequencing of microorganism and invertebrate vectors of disease. The MGSCs provide rapid and cost efficient resources for production of high quality genome sequences of pathogens considered agents of bioterrorism (NIAID category A-C priority list), or causing emerging and re-emerging infectious diseases, their closely related organisms and clinical isolates and invertebrate vectors of disease. | Contracts for Microbial Genome Sequencing Centers have been awarded to The Institute for Genomic Research and the Massachusetts Institute of Technology. |
| NIH | Bioinformatics Resource Centers | NIAID will be funding this fiscal year a number of Bioinformatics Resource Centers (BRCs) for Biodefense and Emerging/Re-emerging Infectious Diseases. The goal is to provide the scientific community with a resource that allows access to genomic and related data for the NIAID category A-C priority pathogens and pathogens causing emerging and re-emerging infectious diseases. Genomic sequence data will be integrated with gene expression (microarray) and proteomics information, host/pathogen interactions and pathways data. Access to these data will be facilitated by a user-friendly web interface and state of the art analysis tools. The BRCs will be supported by multi-disciplinary teams consisting of biologists, pathogen domain experts, bioinformaticians and computer scientists. It is envisioned that these centers will become a major source of information for the NIAID biodefense program and constant interaction and collaboration with the scientific community will be encouraged. | Awards will be made in 2004. |
| NIH | Biodefense Proteomics Research Programs: Identifying Targets for Therapeutic Interventions Using Proteomic Technology | NIAID Proteomic Centers are intended to develop and enhance innovative proteomic technologies and methodologies and apply them to the understanding of the pathogen and/or host cell proteome for the discovery and identification of novel targets for the next generation of drugs, vaccines, diagnostics and immunotherapeutics against microorganisms considered agents of bioterrorism. | RFP-NIH-NIAID-DMID-BAA-03-38 (and 03-45 Administrative Resources for Biodefense Proteomic Centers). Awards will be made in 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Scientific Advance: Malaria Parasite Decoded: Genes May Help to Conquer Deadly Disease | A major scientific achievement for malaria was the publication of the complete genome of this single cell parasite. The relevance of this achievement, which took six years and involved an international team of researchers, is that researchers can now use this genomic information to predict metabolic pathways and to identify gene functions. This information coupled with innovative molecular technologies (e.g. microarrays, proteomics and gene knockouts) enables investigators to validate targets for the development of new drugs and vaccines to treat and prevent infection and disease. Additionally, the genome of this parasite, along with that of the human host and mosquito vector, provides a triad of critical genetic information relevant to all stages of the malaria transmission cycle and offer unprecedented opportunities to the scientific and public health communities engaged in the fight against malaria. | Gardner MJ et al: Genomic sequence of the human malaria parasite *Plasmodium falciparum*. Nature 419:498-511, 2002 |
| NIH | Scientific Advance: Malaria Mosquito, Anopheles gambiae, Sequenced | Anopheles gambiae is the primary mosquito vector of human malaria in Africa. This mosquito has long frustrated researchers because of the difficulty of rearing and manipulating this vector. The publication of the complete genome of this vector has helped spur work in the malaria field. Since the publication of the genome in October, 2002, researchers have made significant progress in defining novel approaches to mosquito control using information obtained during the sequencing and annotation. The genome of this organism, along with the parasite and human genomes, provides a triad of critical genetic information relevant to all stages of the malaria transmission cycle and offer unprecedented opportunities to the scientific and public health communities engaged in the fight against malaria. | Holt RA et al: The genome sequence of the malaria mosquito *Anopheles gambiae*. Science 298(5591):129-149, 2002 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Scientific advance: Genomic sequence analysis provides clues to a pathogens ability to evade antibiotics | Mobile elements embedded in the genome of *Enterococcus faecalis* V58 have enabled the opportunistic pathogen to develop resistance to a range of antibiotics, hence complicating therapy in critically ill patients. Scientists from The Institute for Genomic Research found several of these mobile elements, which are small segments of DNA that can jump from one part of a chromosome to another or from a chromosome in one organism to that of another organism. Nearly a third of the *E. faecalis* genome consists of mobile or 'foreign' DNA. One site is a newly-identified vancomycin-resistance element. The vancomycin resistance genes provide a mechanism for the bacterium to alter its cell wall structure to prevent vancomycin from acting on it. These important findings from the genomic sequence of *E. faecalis* are critical to understanding this medically important organism and will be essential in the search for new antibiotics and vaccines. | Paulsen, I.T., et.al.: Role of Mobile DNA in the Evolution of Vancomycin-Resistant *Enterococcus faecalis* . Science 299:2071-2074, 2003. |
| USDA | Identification and detection of AR genes in intestinal bacteria | ARS developed PCR assays to differentiate among nine classes of tetracycline resistance genes (classes A, B, C, D, E, G, H, K, L) and the assays were validated by using known stock cultures. Three methods for extracting DNA from swine fecal samples were compared and a MoBio commercial kit chosen based on quantity and quality of DNA product. Culture methods for isolating tetracycline resistant bacteria from the swine intestinal tract were developed and used to analyze cecal bacteria from grower stage swine from a farm that has not used antibiotics for growth promotion purposes for at least three years. These methods will be useful to researchers and regulators for measuring antibiotic resistance and developing intervention strategies. | Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center. |
| **Action Item #71: Encourage Sharing of AR Data Between Industry and the Research Community, Including Genomics and Other Technologies.** | | | |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH/DoD | Collaboration on genomics technologies and resources | NIAID continued its agreement with the Defense Advanced Research Project Agency (DARPA) in support of genomics efforts targeted at pathogens of potential bioterrorist threat. | Through this collaboration with DARPA large-scale genome sequencing projects for *Brucella suis* and *Coxiella burneti* have been completed. In addition, DARPA provides funds for the Poxvirus Bioinformatics Resource Center (http://www.poxvirus.org). This resource for the scientific community provides sequencing and functional comparisons of orthopox genes and the design and maintenance of a relational database to store, display, annotate, and query genome sequences, structural information, phenotypic data and bibliographic information. It also serves as a repository of well-documented viral strains. |
| FDA | See Action Item #30: (Anti-Infective Drugs Advisory Committee) | See Action Item #30: (Anti-Infective Drugs Advisory Committee) | See Action Item #30: (Anti-Infective Drugs Advisory Committee) |
| **Action Item #72: Bring New Researchers into the Field, by Utilizing Appropriate Strategies such as Training and Research Opportunities.** | | | |
| FDA | Fellowship Program | Combined Pediatric Infectious Diseases Fellowship formed with Children's National Medical Center, Washington, D.C. | Ongoing: First fellow to complete the program is in June 2004. |
| NIH | Research Scholar Development Award (RSDA)(K22) | The RSDA will provide support for postdoctoral fellows who are moving to assistant professor positions in an academic institution. The purpose of the RSDA is to ease the transition to an academic position by enabling the recipient to focus on the establishment of his/her research laboratory prior to submitting applications for grant support. This is intended to establish new young investigators in needed fields, including AR. | (PAR-02-018) released November 15, 2001; remains active. |
| NIH | Other ongoing training and research fellowship awards | PA-00-003 Mentored Clinical Scientist Development Award (K08) PA-00-004 Mentored Patient Oriented Research Career Development Award (K23) PA-00-005 Mid-career Investigator Award in Patient Oriented Research (K24) | Important ongoing programs are fostering the development of young scientists and clinical investigators. |
| NIH | NIH Exploratory/Developmental Research Grant Award (R21) | This announcement redefines the National Institutes of Health (NIH) Exploratory/Developmental Research Grant Award (R21) mechanism, and extends its use as an investigator-initiated mechanism to a variety of Institutes and Centers (ICs) listed in the announcement. The R21 is intended to encourage exploratory and developmental research projects by providing support for the early and conceptual stages of these projects. | RELEASE DATE: April 18, 2003; expiration date April 18, 2006, unless reissued. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| VA | Proposal Regarding Antibiotic Resistance Fellowship | The Infectious Diseases Program Office proposed the initiation of a two-year VA Special Fellowship in the area of antibiotic resistance at six sites. The proposal required trainees to have completed internal medicine and infectious diseases specialty and subspecialty residency training, and would have required scientific emphasis on antibiotic resistance. | The proposal was rewritten and restructured to focus on training leaders in Terrorism Response for the Future with emphasis on antibiotic resistance. A portion of the training was to include biologic threat agents (including pandemic influenza). |
| **Action Item #73: Organize Conferences That Address Research Issues Relating to AR.** | | | |
| CDC, EPA, FDA, NIH, USDA | National Foundation for Infectious Diseases Conference on Antimicrobial Resistance: Science, Prevention, Control | Scientific conference June 27-30, 2004 in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA. | Organized conference in 2002, 2003, and 2004. |
| FDA, CDC, NIH | Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP) | Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues. | Workshop held April 15-16, 2004. |
| NIH/CDC/FDA | Gordon Conference on Tuberculosis Drug Development | Scientific conference co-sponsored by the Global Alliance for Tuberculosis Drug Development (GATB), the NIAID, and others. The meeting focused on all aspects of new drug development including analyses of the genomic sequences available for mycobacteria, criteria for selection of appropriate drug targets, review of compounds being synthesized, and planning for the development of clinical trial protocols. Investigators involved in all phases of TB drug development from many countries participated in stimulating sessions. In attendance were representatives from the pharmaceutical industry, NIAID, CDC, infectious disease physicians, x-ray crystallographers, chemists, and NIAID-supported research investigators. | Meeting held August 31-September 4, 2003 in Oxford, U.K. |
| NIH | TB Vaccine Regulatory Workshop | Workshop to discuss regulatory aspects and considerations for development of TB vaccines. TB vaccines will be an important component of all strategies for dealing with prevention and treatment of drug resistant TB. Multiple TB vaccine candidates are ready for preclinical development and 2 vaccines, developed with NIAID support, are currently in Phase I clinical trials in the US. In addition to the summary, experience with the preclinical development of these candidates, as well as a candidate evaluated in the UK, contributed to the overall information presented at this meeting. | Meeting was held December 9, 2003 in Bethesda, Maryland. Meeting summary will be posted shortly on: http://www.niaid.nih.gov/dmid/meetings/tbvacc.htm. |
| NIH | The NIAID Pharmaceutical Partners Summit | Meeting to be held in collaboration with the Infectious Disease Society of America in follow-up to NIAID's 2000 Pharmaceutical Summit and will focus on new drug development for resistant infections (http://www.niaid.nih.gov/dmid/drug/summit.htm | Meeting to be held in late summer, 2004 in Washington, D.C. area. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Division of Microbiology and Infectious Diseases Program staff serve as external consultants or liaison to a variety of national and international TB-related groups | Program staff consult and serve as liaison members to national groups, including the Advisory Council for the Elimination of Tuberculosis (ACET) and the CDC TB Clinical Trials and Epidemiology Consortia. International activities include participation on WHO's TB Vaccine Initiative Advisory Committee (TBVIAC), STOP TB Coordinating Board, and the STOP TB Vaccine, Drug and Diagnostic Working Groups. NIAID staff also serves on the Scientific Advisory Committee of the Global Alliance for TB drug Development (GATB). | Ongoing. |
| NIH | A joint meeting of the U.S.-Japan Cooperative Medical Sciences Program, TB and Leprosy Panel | A joint meeting was convened in Newark, NJ on July 21-22, 2003 to foster an exchange of ideas and stimulate international collaborations among U.S., Japanese and other Asian Pacific Rim mycobacterial researchers. For more information about this program: www.niaid.nih.gov/dmid/other/usjapan/DEFAULT.htm | Ongoing. |
| USDA | 2003 Annual Meeting of American Veterinary Medical Association | !/2 day session entitled, "Antimicrobial resistance in Agriculture-practical recommendations". This session highlighted research and possible recommendations for prevention for antibiotic resistance in different food animals (poultry, dairy and feedlot cattle, swine and retail foods) | CSREES organized and moderated session. (July 21, Denver) |
| USDA | Meeting: Impact of antimicrobials on agriculture | USDA (Cooperative State Research, Education and Extension Service; Agricultural Research Service; and Food Safety and Inspection Service) financially supported a research colloquium sponsored by the American Society of Microbiology on the impact of antimicrobials in agriculture in November 2001. This meeting of 35-40 experts provided a forum to discuss the current status, future directions and actions related to the use of antimicrobial resistance in agriculture. The report will be released in Spring/Summer 2002. | Meeting held November 2001. Colloquium report released October 2002 with over 12,000 copies disseminated in 6 months. Obtain from ASM website. |
| USDA | Workshop: A workshop on epidemiologic methods and approaches for food safety | A USDA-CSREES (Cooperative State Research, Education and Extension Service) sponsored workshop, A Workshop on Epidemiologic Methods and Approaches for Food Safety - Fall 2000, included a section on antimicrobial resistance and how to improve methods and approaches to study it. | Meeting held Fall 2001. The proceedings can be obtained from the following website: http:\\www.unl.edu\ianr\vbs\wills\Epiconf |
| USDA | Forum on emerging infections, IOM, NAS | Participated in IOM meeting, The resistance phenomenon in microbes and infectious disease vectors - Implications for human health and strategies for containment. Proceedings (www.nap.edu). | Complete. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | AR and impact on agriculture | Roundtable presentation at ASM annual meeting, May 2002, Salt Lake City, UT. Provided overview of ASM research colloquium on impact of antimicrobials in agriculture. | Complete. |
| **Action Item #74: Explore the Need To Encourage Preclinical Studies on the Toxicology, Pharmacokinetics of Novel Therapeutic Agents for the Treatment of Multidrug-Resistant Pathogens And Facilitate the Transition of Potential Products from Preclinical to Clinical Studies Leading to Development by Industry of Novel Therapeutic Agents.** | | | |
| NIH | Pharmacokinetics & Pharmacodynamics of Antimicrobials in Animal Models Request for Proposals | The purpose of this contract is to stimulate research towards discovery of improved therapies for TB. The emergence of multidrug resistant tuberculosis has produced sizable medical challenges to the treatment and containment of infectious tuberculosis in the face of limited chemotherapeutic options. In order to facilitate the development of improved drugs for the treatment of TB, and particularly multidrug resistant TB, the NIAID requires the directed evaluation of selected novel synthetic and pure natural product compounds. This contract will provide critical support for investigator-initiated drug discovery, stimulate private sector sponsorship of new drugs, perform comparison (or confirmatory) studies from different sponsors, and provide information for selection of antimicrobial drug candidates for design of clinical studies. It will serve as the central facility for evaluation of novel compounds for physical, pharmacokinetic, and pharmacodynamic properties. | Award to be made in 2004. |
| NIH | Respiratory Pathogens Research Network | The Respiratory Pathogen Research Units (RPRU) form the basis of a coordinated, interactive, multi-disciplinary network to help support preclinical and clinical studies against selected human respiratory pathogens which include pneumococci, Group A Streptococci and Group B Streptococci. The focus will be the conduct of pre-clinical research activities that are designed to validate or lead to clinical studies and related clinical trials of candidate vaccines and therapeutics. | In 2003 a Bacterial Respiratory Pathogens Research Unit was awarded at the University of Iowa. |
| **** TOP PRIORITY **** | | | |
| **Action Item #75: In Consultation with Academia and the Private Sector, Identify and Conduct Human Clinical Studies Addressing AR Issues of Public Health Significance That Are Unlikely To Be Studied in the Private Sector.** | | | |
| FDA, CDC, NIH | Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP) | Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues. | Workshop held April 15-16, 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH, NIAID | Division of AIDS Clinical Trials | Numerous trials underway: R. Semba, Johns Hopkins University, “Adjunct Vitamin Therapy for Tuberculosis and HIV/AIDS in Malawi.” R. Chaisson, Johns Hopkins University, “Novel TB Prevention Regimens for HIV-Infected Adults” in South Africa. C. Whalen, Case Western Reserve, “Randomized, Phase II Study of Punctuated Antiretroviral Therapy for HIV Infected Patients with Active Pulmonary Tuberculosis and CD4 count > 350 cells/mm3.” S. Abdool Karim, University of Natal, South Africa “Collaborative AIDS Programme of Research in South Africa. | Ongoing clinical trials that will be monitoring for resistance. |
| NIH | Tuberculosis Research Unit (TBRU) | The TBRU contract (N01-AI-95383, Case Western Reserve University) continues to make progress in developing surrogate markers of disease and human protective immunity and in conducting clinical trials of potential new TB therapeutic, preventive, and diagnostic strategies. Furthermore, well-characterized clinical samples will be available for distribution to TBRU investigators and their collaborators through a newly established repository. Activities of the TBRU are coordinated with other major organizations involved in TB research, including the CDC, USAID, FDA, WHO, Global Alliance for TB Drug Development and IUATLD, and with interested industrial partners. | Information about on-going TBRU supported studies can be found at: http://www.tbresearchunit.org. The TBRU is currently undertaking a clinical trial to evaluate the potential of Fluoroquinolone drugs to be used as anti-TB agents. |
| NIH | Bacteriology and Mycology Biostatistical and Operations Unit (BAMBU) | This contract supports study planning, protocol design, development, implementation, training, safety monitoring, data management and analysis, site monitoring, manuscript preparation, and other necessary and regulatory activities of clinical trials conducted through the BAMSG (see item above) contract. | Ongoing. |
| NIH | Vaccine and Treatment Evaluation Units (VTEUs) | The VTEUs are a network of university research hospitals across the United States that conduct Phase I, II, and III clinical trials to test and evaluate vaccine and therapeutic candidates for infectious diseases. Through these sites, researchers can quickly carry out safety and efficacy studies of promising vaccines in children, adult, and specific high-risk populations. The results of these trials may have a profound effect on public health here and abroad. Through numerous studies at the VTEUs, researchers have tested and advanced vaccines for malaria, tuberculosis, pneumonia, cholera, and whooping cough. In the last 6 years alone, NIAID has supported more than 110 clinical trials through the VTEUs. | Seven VTEUs were awarded in June 2002: Baylor College of Medicine, Cincinnati University Children’s Hospital Medical Center, UCLA Center for Vaccine Research, St. Louis University Health Sciences Center, University of Maryland School of Medicine; University of Rochester School of Medicine and Dentistry, and Vanderbilt University Medical Center. VTEUs will conduct clinical trial work on two new anti-TB vaccines in partnership with Corixa Corp. (fusion protein vaccine) and UCLA/Sequella Global TB Foundation (recombinant BCG vaccine). Both candidate vaccines were originally developed with NIAID grant support. http://www.niaid.nih.gov/factsheets/vteu.htm. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Prevention of group B streptococcal (GBS) disease contract | NIAID continues to support research on the prevention of group B streptococcal disease through a five year multidisciplinary contract awarded late in 2002 to the Channing Laboratory, Brigham and Women's Hospital. This collaborative multidisciplinary effort is focused on clinical studies in selected populations to further understand GBS infection and on studies of the host immune response. | A clinical trial was initiated to evaluate the impact of a GBS vaccine on GBS colonization that had implications for reducing the amount of antibiotics administered to pregnant women during delivery. |
| VA | VA research update | VA investigators have a rather extensive portfolio in antibiotic resistance research that for fiscal year 2000 identifies twenty-three separate funded proposals in AR. For 2001, there are twenty-nine funded projects related to AR by VA investigators. These funded research grants cover a wide spectrum of AR issues. In addition, these do not include large clinical trials that may have impact on AR such as collaboration with the NIH-funded HIV ACTG's and pharmaceutical corporate-related research that is widespread throughout the VHA. A specific area of emphasis is transmission of resistance among organisms and spread of these organisms from person to person. Such topics as spread of resistance in nursing homes, the relationship of resistance to staffing levels, and work practices (organization) as they relate to antibiotic resistance are all part of VA investigators' portfolios and are topics unlikely to be studied in the private sector. VA investigators continue to have an extensive and expanding portfolio in antimicrobial resistance research. | Ongoing. In 2001, twenty-eight projects related to bacterial resistance were underway, an increase of over 300% from 1997. Ongoing. In 2002, VA provided an increase in funding for projects related to AR of approximately 62% when compared to 2001. The number of studies receiving VA-funded financing increased by 80% when comparing 2002 to 2001. VA funding for bacterial antimicrobial resistance related research increased by 90.6% when comparing 2003 to 2001. |
| **** TOP PRIORITY ****<br>**Action Item #76: Identify, Develop, Test, and Evaluate New Rapid Diagnostic Methods for Human and Veterinary Uses with Partners, Including Academia and the Private Sector. Such methods Should Be Accurate, Affordable, and Easily Implemented in Routine Clinical Settings.** | | | |
| CDC | *C. trachomatis* resistance | Chlamydia trachomatis causes a sexually transmitted infection in an estimated 3 million Americans annually; untreated women can develop pelvic inflammatory disease, which can lead to chronic pelvic pain, infertility, and potentially fatal ectopic pregnancy. Several methodologies are used to assess antimicrobial susceptibility among C. trachomatis isolates, and this project will compare those that are currently used in an attempt to develop a standardized/reproducible assay that can be utilized for monitoring treatment efficacy. | Preparing a report on a meeting of external consultants (which took place prior to 2002) and organized an international meeting to be held in conjunction with International Society for Sexually Transmitted Diseases Research (ISSTDR) on July 30, 2003 to share our preliminary meeting report and dialogue about further problem-solving. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Test kit evaluation | Work to develop streamlined mechanisms for evaluating rapid diagnostic test kits for identifying microbes and for determining susceptibility to treatments. Work with academia and industry to produce guidance documents and reference methods that could be used in evaluating new rapid diagnostics for use in the clinical setting. | FDA sponsored SARS workshop in July 2003 to exchange information on assays for rapidly emerging challenges, how to facilitate pathways for fiedling new assays; and incorporate new assays into clinical & public health use. Participants included FDA, NIH, CDC, WHO, China, Taiwan, Hong Kong, & Canada. IDE for SARS approved for CDC PCR assay. Cleared 3 West Nile Virus in vitro diagnostic devices. Cleared first in vitro diagnostic test for direct detection for nasal colonization by methicillin-resistant *Staphylococcus aureus* . Cleared first of a kind test using sputum & nucleic acid amplification for direct detection of Legionella pneumophilia DNA, intended to aid in presumptive diagnosis of Legionnaires' disease in conjunction with culture. Ongoing: Working with ISO/TC 212 WG 4 on Antimicrobial Susceptibility Testing (AST). The projects are to develop ISO requirements for a reference method for AST & evaluation of performance of AST devices in cooperation with the European Committee for Standardization (CEN). |
| FDA | Rapid diagnostic methods to detect multi drug resistant TB (MDRTB) strains | Research: development of rapid diagnostic methods for detecting MDRTB based on the microarray technology. | Collaboration of CDRH with CBER. |
| FDA | New rapid diagnostic methods | Research: new rapid diagnostic methods for bacterial contamination of foods. | Collaborating with CFSAN research. Developed new detection method using antibodies attached to chip. Working to establish limits of detection and apply to variety of foodborne agents. |
| FDA | Surveillance activities | Coordinate surveillance activities with CDC. | Held initial meeting with CDC April 25, 2001; further discussions ongoing. |
| FDA | Nucleic Acid Tests (NAT) for detection of bacteria in donated blood products | Research: Development of nucleic acid tests (NAT) based on PCR-test, TaqMan assay and DNA microarray to detect transfusion induced sepsis causing gram positive and gram negative bacteria potentially present in donated blood products. This technology can be easily adapted to detect bloodborne antibiotic resistant bacteria. | Ongoing project: Awarded Director's Targeted Research Grant, CBER, FDA. |
| NIH | Biodefense and Emerging Infectious Diseases Research Opportunities | In response to growing concerns about the use of biological agents in acts of terrorism, NIAID has expanded its biodefense research program. The Ultimate goal of that expansion is to develop effective diagnostics, vaccines and therapeutics to protect the public in the event of a biological attack or the sudden emergence of select rare or eradicated diseases. | Notice AI-02-023; http://grants1.nih.gov/grants/guide/notice-files/NOT-AI-02-023.html. In 2003 converted to PA-03-080; expires March 2006 http://grants1.nih.gov/grants/guide/pa-files/PA-03-080.html. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Biodefense Partnerships: Vaccines, Adjuvants, Therapeutics, Diagnostics, and Resources. | It is imperative that candidate vaccines, therapeutics, adjuvants, diagnostics and resources against selected infectious biological threat agents be developed as quickly as possible to reduce the threat of their use in acts of terrorism or war. The interaction of industry or non-profit organizations with academic organizations (if applicable) and the Government is strongly encouraged to quickly transition candidate products through preclinical development and clinical testing and commercialization. This partnership program will support the clinical development of specific high priority products beginning with the further characterization of the candidate through preclinical development and Phase I and/or Phase II clinical studies. | RELEASE DATE: November 14, 2002 (see NOT-AI-03-006), Program Announcement: PAR-03-025; awards include a project entitled "Novel Antibacterial Agents for Treatment of Tularemia." |
| NIH | Partnerships for Novel Therapeutic, Diagnostic, and Vector Control Strategies in Infectious Diseases (PAR 02-026) | The objective of this program is to support the development of drugs and diagnostics for human infectious diseases of public health importance and products for controlling arthropod vectors that transmit infectious agents. This PAR emphasizes areas that could have a high impact on public health, but currently appear not to be a high priority or that may be considered too financially risky for industry. In addition, research on agents of bioterrorism concern are of high priority. Projects supported should have the ultimate goal of producing a novel therapeutic, diagnostic tool, or vector control agent or strategy that adds substantively to the current armamentarium for control of an infectious disease that causes a significant public health burden but is not a current priority for industry research and development. | Multiple awards made in 2003; awards include: "PEGylated Lysostaphin for Staphylococcal Infections" |
| NIH | Partnerships for Vaccines and Diagnostic Development | A Request for Applications (RFA 03-028) entitled “Partnerships for Vaccines and Diagnostic Development” was released on June 9, 2003. This RFA is focused on development of vaccines against GAS, GBS and Helicobacter pylori and point of care diagnostics for GAS and GBS. Cooperative agreements (U01s) will be used to support the research which must include substantive involvement by an industry partner. | Approximately 6-10 awards will be made in 2004 |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Development of a rapid, sensitive and specific PCR-based test for detecting multiple AR Salmonella typhimurium DT104 (DT104) | ARS developed this test to provide the basis for rapid pre- and/or post-harvest detection of an important foodborne pathogen. The implementation of this test will reduce the time needed to detect DT104 from 24- 48 hours to 8-12 hours. That is, potentially contaminated meat could be detected before leaving the slaughterhouse. This system was combined with a similar test for E. coli O157:H7 so that both pathogens could be detected simultaneously. | Completed: USDA-ARS: Ames, IA - National Animal Disease Center (NADC). |
| USDA | New methods for the determination of AR in Campylobacter | Antimicrobial test methodologies for Campylobacter are technically difficult, costly and often difficult to compare to agar dilution which is considered the 'gold standard'. A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in Campylobacter species. This work will be presented to the National Committee for Clinical Laboratory Standards (NCCLS) for adoption as a recommended testing methodology. NCCLS determines the most accurate means of antimicrobial susceptibility testing and disseminates this information worldwide. | Completed USDA-ARS: Athens, GA. |
| USDA | Identification of collagenase secreted by *Salmonella typhimurium* DT 104 and the development of a RT-PCR assay for collagenase expression | In a recent study, we identified a collagenase secreted by DT104. The collagenase identification was based on DNA sequence homology to an E. coli collagenase. Also, we could reconstitute the cytotoxic phenotype by introducing the collagenase gene into a collagenase(-) strain. This collagenase is expressed and secreted only under certain conditions that seem to be determined by the host. We have developed an RT-PCR assay for collagenase expression, and we will be using this assay to identify other strains that exhibit the cytotoxic phenotype. | Ongoing. NADC, Ames IA |
| USDA | Develop pre-harvest version of the USDA-FSIS FAST | The University of Nebraska will develop a more cost-effective test for detecting antibiotic-resistant bacteria. Educational materials will also be produced. | Ongoing. Griffins, University of Nebraska.<br>Funded through CSREES, National Integrated Food Safety Initiative 111 |
| USDA | Development of a rapid PCR assay for genus and species identification of enterococci | We developed a multiplex PCR procedure in conjunction with a colony PCR method that will identify the genus and the species of 25 Enterococcus strains that have been isolated and classified. Primers specific for the genus have been combined in 7 different reaction mixtures to primers for the different species and from bacterial culture to finish, the entire process requires approximately 3 ½ hours. The procedure is a cost-effective, rapid, and accurate method for identification of enterococci and an application for a patent is currently being pursued. | Ongoing. Russell Research Center, Athens, Georgia. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Factors affecting microbial ecology of pathogen colonization and AR acquisition | An automated ribotyping system is being used at the USDA/ARS FFSRU to identify, characterize and monitor gut bacteria isolated by us and others; information obtained from this use is being maintained in the Gastrointestinal Microflora Ribotype Database (GMRD). Molecular typing methods (e.g. ribotyping, denaturing-gradient gel electrophoresis (DGGE), and DNA sequencing) are being used to distinguish bacterial strains inhabiting the gastrointestinal tract with even greater precision and to determine genetic alterations occurring within these bacteria. This database is being used by scientists worldwide to develop a more thorough understanding of the effects of sub-therapeutic antibiotic administration and other stressors on the ecology of the gut microflora. | Ongoing. Food and Feed Safety Research Unit, ARS, College Station, TX. |
| USDA | Evaluate a microbroth dilution assay for antimicrobial susceptibility testing of Campylobacter | A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in Campylobacter species. This assay provides an alternate means for testing large numbers of Campylobacter for resistance to a panel of antimicrobials. This work will be useful to scientists and clinicians involved in assessing antimicrobial resistance. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| USDA | Develop a PCR assay for detection of mixed cultures in Campylobacter | Testing for antimicrobial resistance typically occurs on bacteria originating from one single colony. It is commonly assumed that this single colony arose from one bacterium. However, recent reports suggest that bacteria may aggregate, making selection of a single bacterium difficult. We developed a PCR assay which identifies mixed populations of Campylobacter. This PCR assay is ideal for applications with high throughput requirements, such as often occurs within our laboratories testing bacteria for resistance to antimicrobials. This work will be useful to scientists and clinicians involved in assessing antimicrobial resistance. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| USDA | Develop a rapid PCR assay for genus and species identification of Enterococci | The current classification and identification scheme for Enterococcus is both tedious and laborious and is based upon phenotypic analysis and there is no procedure that will allow genus and species identification of enterococci in less than 24 hours. To this end, scientists in our Unit have developed a multiplex PCR procedure in conjunction with a colony PCR method that will identify the genus and the species of 25 Enterococcus strains that have been isolated and classified. Primers specific for the genus have been combined in 7 different reaction mixtures to primers for the different species and from bacterial culture to finish, the entire process requires approximately 3 ½ hours. The procedure is a cost-effective, rapid, and accurate method for identification of enterococci. This work will be useful to scientists involved in Enterococcus research. | Completed. Antimicrobial Resistance Research Unit, ARS, Athens, GA. |
| **Action Item #77: Encourage Basic and Clinical Research in Support of the Development and Appropriate Use of Vaccines in Human and Veterinary Medicine in Partnership with Academia and the Private Sector.** | | | |
| NIH, USAID | Randomized, double-blinded, controlled Phase III efficacy trial of pneumococcal conjugate vaccine | NIAID is conducting a randomized, double-blind, controlled Phase III efficacy trial in Gambia, West Africa, using a 9-valent pneumococcal conjugate vaccine manufactured by Wyeth-Lederle Vaccines and Pediatrics (WLVP). The trial is designed to determine the impact of the pneumococcal conjugate vaccine, when administered with DPT/Hib (TetramuneTM) in the same syringe, on childhood mortality due to invasive pneumococcal disease. The main endpoint will be overall mortality; however, secondary endpoints will include the effect of the vaccine on mortality and on invasive pneumococcal disease caused by pneumococci of vaccine serotype. Approximately 16,000 children will be recruited into the trial from shortly after birth over a period of 3 and a half years. Three doses of the DTP/Hib vaccine mixed with the 9-valent pneumococcal conjugate vaccine will be administered to half the children at two, three, and four months of age. The other half will receive just the DTP/Hib vaccine. | Preliminary efficacy results are expected in late 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| CDC | Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP) | A 7-valent conjugate vaccine for *Streptococcus pneumoniae* , licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Four CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in nine Emerging Infections Program areas in which population-based active surveillance is conducted. Second, ongoing active surveillance in these areas will track any change in the amount of invasive disease due to drug resistant strains. The third project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The fourth is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees. | Ongoing. During 2000 and 2001 the case control study protocol was developed, a pilot study was launched, and procedures manuals and tracking system were revised in preparation for the main study. During 2002, cases and controls were enrolled and main data collection began. In 2003, we completed enrollment for children <2 years and are finishing enrollment of children 2-4 years in 2004. Preliminary analysis indicates that the vaccine is very (>90%) effective against disease caused by pneumococcal serotypes in the vaccine and serotypes closely related to those in the vaccine. ABCs surveillance indicates that by 2003 disease due to penicllin-resistant strains had dropped by over half. (Whitney CG, et al. N Engl J Med 2003 May 1;348(18):1737-46). In Anchorage, 4 consecutive carriage studies have been completed. While analysis is ongoing, preliminary results suggest that carriage of strains resistant to trimethoprim/sulfamethoxazole has become less common while carriage of penicillin resistant strains has not changed. |
| DoD | Double-blind placebo-controlled clinical effectiveness trial of the 23-valent pneumococcal vaccine | *S. pneumoniae* is a leading cause of morbidity in the U.S., causing an estimated 500,000 cases of pneumonia, 3,000 cases of meningitis, 50,000 cases of bacteremia, and 7,000,000 cases of otitis media annually. Data from 1981 to 1991 suggest that *S. pneumoniae* causes approximately 12% of pneumonia hospitalizations in the military or 9.5 admissions per 100,000 person-years. A 23-valent pneumococcal vaccine is being used at one military basic training facility and at military training facilities. This vaccine provides coverage for 85 - 90% of the serotypes causing bacteremia in the general population, but its clinical benefit needs to be more fully characterized before the impact of its use on the emergence or spread of S. pneumoniae resistance can be determined. | Ongoing. Enrollment was completed in June 2003, with a total of 152,765 recruits enrolled. Data analysis is ongoing. Preliminary results will be presented at the 4th International Symposium on Pneumococci and Pneumococcal Diseases in May of 2004. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Vaccine research | Research in support of the development and appropriate use of vaccines in humans to: 1) prevent viral infections, i.e. influenza, RSV; 2) prevent common bacterial infections i.e. *S. pneumoniae*, non-typable *Haemophilus influenzae*, group B streptococcus, *N. gonorrhoeae, N. meningitidi*s. | Twelve ongoing research projects support development of vaccines for the organisms listed:<br>1) Completed study of protective levels of antibody against neonatal type 1a and 3 group B streptococcal infection (funded through interagency agreement with NICHD).<br>2) Ongoing research regarding correlates of protection against other common types of group B streptococcus. 3) Investigating correlates of protection against infection with *Streptococcus pneumonia*.<br>4) N. gonorrhoeae. Studying immunogenicity and pathogenicity of associated proteins, funded through the FDA Office of Women's Health. |
| FDA | Vaccine development | Research in support of the development of vaccines to prevent colonization, infection, and transmission of tuberculosis | Current projects investigate the following vaccine candidates in mouse model of tuberculosis: combination DNA vaccines, multigene DNA constructs, attenuated live vaccines and subunit vaccines. These vaccines are also being tested using prime-boost strategies and post-exposure models. |
| FDA | Multidrug resistant TB | Research: mechanisms of resistance in multidrug resistant tuberculosis. | Identified genetic mechanisms for multiple mechanisms of drug resistance in *M. tuberculosis*. |
| FDA | Drug therapy | Research: novel targets for drug therapy (to avoid resistance). | Two ongoing projects that examine the mechanisms of development of HIV drug resistance. |
| NIH | Phase One safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults with booster sub-study | NIAID is the sponsor of a Phase 1 safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults, 50-85 years old. A subset of 50-64 year-old volunteers received a booster dose approximately six months after the first dose. The vaccine was well tolerated in all volunteers. | Future plans include serological testing and data analysis. |
| NIH | Double-blind, randomized, controlled multi-center trial in older adults to an experimental 9-valent conjugate pneumococcal vaccine compared with the conventional 23-valent pneumococcal polysaccharide vaccine | Elderly individuals are at an increased risk for serious pneumococcal infection. Understanding and improving the response to pneumococcal vaccine in persons over the age of sixty-five is an important step in preventing this serious illness. To address this issue, a double-blind, randomized, controlled multi-center trial was conducted to evaluate the relative safety and immune response to an experimental 9-valent conjugate pneumococcal vaccine compared with the conventional 23-valent pneumococcal polysaccharide vaccine in older adults. The response to revaccination following conjugate vaccine is also being evaluated. Outcome measures include adverse effects, serotype specific antibody responses as well as antibody responses to carrier protein, effects on functional antibody status and on nasal carriage of S. pneumoniae. | Early results indicate that the conjugate vaccine is well tolerated and generates no greater local reactions than the licensed polysaccharide vaccine. Individuals challenged with the polysaccharide vaccine following a single dose with the conjugate demonstrate higher antibody levels to 8 of 9 serotypes compared to individuals who first received 2 doses of the conjugate vaccine or just the polysaccharide vaccine alone. The data suggest that a pneumococcal conjugate vaccine may prime for a more robust response to subsequent exposure to a licensed polysaccharide vaccine. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Partnerships for Vaccines and Diagnostic Development | A Request for Applications (RFA 03-028) entitled “Partnerships for Vaccines and Diagnostic Development” was released on June 9, 2003. This RFA is focused on development of vaccines against GAS, GBS and Helicobacter pylori and point of care diagnostics for GAS and GBS. Cooperative agreements (U01s) will be used to support the research which must include substantive involvement by an industry partner. | Approximately 6-10 awards will be made in 2004. |
| NIH | Vaccine Action Program | The INDO-US Vaccine Action Program initiated in 1987 is a bilateral program that focuses on the development of safe and effective vaccines for major communicable diseases of interest to the two countries through joint research and development efforts. | Priorities under VAP include issues such as: acute respiratory illness, group A streptococci, hepatitis, diarrhea caused by Rotavirus, cholera and other infectious agents, leishmaniasis, typhoid, rabies, HIV/AIDS, tuberculosis, malaria, malnutrition and emerging and re-emerging infectious diseases. |
| NIH | Adult efficacy trial using acellular pertussis vaccine | An adult efficacy trial using acellular pertussis vaccine was recently completed in 2,784 subjects 15-65 years of age to define the incidence, clinical spectrum, and epidemiology of pertussis infection and disease in adolescents and adults as well as define the safety, immunogenicity, and efficacy of an acellular pertussis vaccine designed for use in older individuals. The acellular vaccine was shown to be safe with no vaccine associated serious adverse events. Confirmed pertussis occurred in two vaccines and 9 controls, yielding an efficacy of 77%. This estimate of efficacy is similar to that observed in young children. | These data suggests that an acellular pertussis vaccine given to adolescents and adults in the form of a dTaP booster would be safe and effective in reducing the burden of disease in this population in addition to reducing secondary transmission to infants. |
| NIH | Phase I Malaria vaccine trial | NIAID, in collaboration with Walter Reed Army Institute of Research (WRAIR), GlaxoSmithKline Biologicals, the UMd/CVD, and the University of Bamako, Mali, is supporting a Phase 1 trial in Mali of a novel candidate vaccine that targets the blood-stage of malaria parasites. | Ongoing. |
| NIH | Phase I Malaria vaccine trial | In collaboration with Apovia, Inc., a biotechnology company, NIAID has undertaken a Phase 1 trial of a novel pre-erythrocytic stage, candidate malaria vaccine at the University of Maryland Center for Vaccine Development (UMd/CVD). This vaccine was developed with grant support from the SBIR Program administered at NIAID, and with additional support and collaboration from the Malaria Vaccine Initiative supported by the Program for Appropriate Technology (PATH). Results of this initial trial are expected to be available for analysis in 2004. | Ongoing. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Millennium Vaccine Initiative-Novel Vaccines for Tuberculosis and Malaria (RFP AI 02-15) | The goal of this contract solicitation is to increase collaboration between industry and the public sector to promote the development of new vaccines to prevent tuberculosis and malaria in developing countries using existing technology platforms. | In 2003, one award made to Epimmune, for development of a novel malaria vaccine in collaboration with NIAID and the Naval Medical Research Center, and one award made to Corixa Corporation for development of optimized delivery methods and adjuvants for TB vaccines. |
| NIH | TB Structural Genomics Consortium | This consortium is co-funded by NIGMS and NIAID, was initiated in 2000 and seeks to determine the three-dimentional structure of over 400 functionally relevant proteins from M. tuberculosis. As of 2003, the consortium consists of over 130 laboratories in 65 institutions from 14 countries. Crystal structures of essential pathogen proteins greatly facilitate drug development and compound optimization efforts. | Award made for 5 years to the Los Alamos National Laboratories with key collaborations from other institutions. |
| **Action Item #78: Encourage Basic and Clinical Research in Support of Novel Approaches to Preventing or Treating Infections with Resistant Organisms That Occur in Humans and Animals by Partnering with Academia and the Private Sector.** | | | |
| CDC, NIH, USAID | Global Alliance for TB Drug Development | The Global Alliance for TB Drug Development is a new public/private partnership to stimulate new drug development against tuberculosis. NIAID is involved in this collaboration with private partners, who are contributing to the development of new drugs to shorten the treatment of TB and facilitate its control in the poorest countries. Over 30 organizations are stakeholders in this innovative public-private partnership, including the Bill & Melinda Gates Foundation, CDC, NIAID/NIH, Rockefeller Foundation, USAID, the World Bank, and WHO. For a comprehensive list, see: http://www.tballiance.org | Program staff assist the GATB in the process of soliciting requests for drug discovery and development proposals from the global research and development community and in the scientific peer review of the received proposals. As part of a broad search for new collaborations and new drug candidates, program staff and GATB representatives attended meetings with pharmaceutical companies with compounds or drugs showing promise as new TB drugs. Staff hold memberships and chair of the Scientific Advisory committee and NIAID TB contract resources contributed significantly to the pre-clinical development of a new TB drug candidate, PA-824. |
| NIH, NSF, USDA | International Cooperative Biodiversity Groups Program (ICBG) | International Cooperative Biodiversity Groups Program (ICBG) has a 3 fold mission: conservation of biodiversity, economic growth for developing countries, and discovery of pharmaceuticals from natural products. The ICBG program is a model for research partnerships by acknowledging intellectual property ownership of indigenous communities. | A continuation of the International Cooperative Biodiversity Groups was announced (ICBG; http://grants2.nih.gov/grants/guide/rfa-files/RFA-TW-03-004.html) to address the interdependent issues of biodiversity conservation, economic capacity, and human health through discovery and development of therapeutic agents for diseases of importance in developing countries as well as those important to developed countries. Planning grants and comprehensive awards are expected to be made in FY04. |
| FDA | Guidance document | Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals | Working group formed; Draft document completed. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Challenge Grants (RFA AI-00-010) | Through a special appropriation from Congress in 2000, a new government/industry partnership was set up with industry matching NIAID funds 1:1, using milestone-driven goals for evaluation and allowing substantive involvement on the part of NIH. NIAID funds are being matched with industry funds from Sequella Inc. to develop improved drugs for TB treatment, Glaxo SmithKline to develop drug candidates against TB and other bacterial infections, and Corixa Corp. to conduct preclinical testing of new TB candidate vaccines. | Ongoing. The vaccine candidate developed by Corixa Inc. in partnership with GSK under this challenge grant is now being evaluated in clinical trials in humans. Sequella, Inc. has developed promising derivatives of Ethionamide and are considering preclinical development of a lead candidate. |
| NIH | Pharmaco-economics report on TB drug development | Through participation in the Global Alliance for TB Drug Development, many NIAID-supported investigators and staff contributed to a publication detailing the investments and potential markets required to develop a new drug for the treatment of TB. The NIAID TB Technology Transfer contractor (Research Triangle Institute of North Carolina) organized, researched, coordinated, and edited a major report on the economic factors involved in bringing a new anti-tuberculosis drug to market. This report continues to be a rigorous, authoritative source of information on the epidemiology of TB, potential market for new anti-TB drugs, cost of TB drug development, and options for funding and conducting drug development. The report provides data required for informed investment decisions by industry, foundations, government organizations, and world health and financial organizations. | Available on the Global Alliance for TB Drug Development website, http://www.tballiance.org. |
| NIH | Anti-Infective Drug Development Contracts are testing new medicines | Research and development contracts are actively testing new candidate compounds for efficacy against infectious complications of AIDS in culture and in animals, a critical component in new drug development and approval. The contract resources will allow NIAID to support: (1) investigator-initiated drug discovery; (2) to stimulate private sector sponsorship of new drugs; (3) to perform comparison or confirmatory studies from different sponsors; and (4) information for selection of anti-mycobacterial drug candidates and for design of clinical studies. | Six Contracts are supported under this program. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF) | New drugs to treat TB are being screened through this NIAID contract. Southern Research Institute in Birmingham, Alabama has established a facility to acquire compounds for screening against Mtb, maintain a computerized chemical database of compound structures, coordinate and distribute compounds for evaluation in vitro and in an animal model, and report data back to suppliers. | The TAACF has contacted over 3,500 chemists throughout the world seeking candidate anti-TB compounds. Over 60,000 compounds have been received from academic and private sector investigators, principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites; more than 200 unique chemical entities are in the queue for evaluation for safety and efficacy in animal models of infection, and for activity against resistant strains of M. tuberculosis.<br>http://www.taacf.org. |
| NIH | Submission of compounds for in vitro evaluation | Staff have selected for evaluation more than 10,000 compounds, based on their chemical structure, from the National Cancer Institute (NCI) chemical repository of over 500,000 compounds. Of these compounds, 500 have shown initial in vitro activity against a wild-type strain, and of these, approximately 100 have promising in vitro activity against isoniazid (INH)-resistant strains. A large part of this effort is conducted under an interagency agreement with the Health Resources and Services Administration at the Gillis W. Long Hansen's Disease Center. Efficacy evaluations in animal models of TB are being conducted on selected compounds. | Ongoing. NIAID chemists continue to evaluate novel compounds from existing government compound repositories for potential activity against wildtype and resistance M. tuberculosis. |
| NIH | High-throughput screening contract (N01-AI-15449) with Southern Research Institute | This contract awarded to Birmingham, Alabama in response to RFP AI01-13, "Tuberculosis Drug Screening: Part B" will provide a high throughput screening capability to develop and implement biochemical, target-specific Mtb drug screening assays and to develop and implement Mtb metabolic stage-specific drug screening assays. | Ongoing. Selected molecular targets are being screened against large chemical libraries to identify new candidate antibiotics as potential additions to the combined regimen for treatment of tuberculosis, particularly to combat multidrug resistant strains. |
| NIH | Therapeutics Research on AIDS-Associated Opportunistic Infections and Malignancies | The goal of this program is to stimulate iterative preclinical research for novel therapeutic strategies against opportunistic infections, co-infections, and malignancies in people with HIV/AIDS. The PA is a joint sponsorship with the National Cancer Institute and the National Institute of Dental and Craniofacial Research. The AIDS-associated infections emphasized by this PA are tuberculosis, Pneumocystis carinii pneumonia, Cryptosporidium parvum, and the microsporidia. The AIDS-associated malignancies emphasized by this PA are Kaposi's sarcoma, lymphomas, cervical cancer, oral warts and cancers, and anogenital cancers. | PA-01-113 grants awarded in 2003 on TB:<br>o W. Bishai (Johns Hopkins University) Toolbox for Tuberculosis Drug Development<br>o R. Slayden (Colorado State University) Regulation of Cellular Division in M. tuberculosis<br>o W. Suling (Southern Research Institute-Birmingham) FolK, a Mycobacterium tuberculosis Drug Target<br>o L. Heifets (National Jewish Medical and Research Center) Nanoparticles Delivery System for Antituberculosis Drugs<br>o R. Li (Southern Research Institute-Birmingham) Novel Antifolates Against AIDS-Associated Tuberculosis |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| NIH | Four National cooperative drug discovery groups (NCDDG-OI) are working on TB drug discovery | In order to stimulate private sector involvement in the development of drugs for TB, three NCDDTG (P. Brennan, Colorado State University; L. Heifets, National Jewish Center; W. Jacobs, Albert Einstein University; J. Sacchettini, Texas A&M University) actively collaborated with pharmaceutical firms with an interest in TB drug development (Glaxo SmithKline). A fourth NCDDG is studying the Mtb alanine racemase for targeted drug design (Kurt Krause, University of Houston). | Collaborations ongoing. |
| NIH | Pharmacokinetics and Pharmacodynamics of Antimicrobials in Animal Models | This contract will allow the NIAID to provide critical support for investigator-initiated drug discovery, to stimulate private sector sponsorship of new drugs, to perform comparison (or confirmatory) studies from different sponsors, and to provide information for selection of antimicrobial drug candidates for design of clinical studies. This contract will serve as the central facility for evaluation of novel compounds for physical, pharmacokinetic, and pharmacodynamic properties. | Award to be made in 2004. |
| NIH | Scientific Advance: Moxifloxacin is a promising new antibiotic for tuberculosis | Moxifloxacin is a new quinolone antibiotic shown to have potent bactericidal activity against TB in an animal model of acute infection. Daily dosing of the antibiotic in levels equivalent to those used in humans reduced the levels of TB in the spleens and lungs of infected mice. The effect was comparable to isoniazid (INH) – one of the most potent drugs ever discovered to treat tuberculosis. The maximum bactericidal effect was seen with daily doses of 400 mg/kg, whereas weekly dosing was not as effective. Because of the favorable pharmacokinetic properties of moxifloxacin, this advance suggests that in combination with other longer acting antibiotics, the potential exists to shorten the course of antituberculous therapy or to allow more intermittent (i.e., once-weekly) therapy. Further studies are planned to explore this possibility in the mouse model of TB and in controlled human clinical trials. This product may provide additional options for treating MDR TB that would increase therapy compliance. | These experiments and further long term animal evaluations of moxifloxacin as a potential sterilizing addition to standard TB therapy are contributing to design of new human clinical trials. Award Data: R01 AI43846; W. Bishai, Johns Hopkins University " |

**Focus Area IV: Product Development**

**** TOP PRIORITY ****

**Action Item #79: Create An Interagency AR Product Development Working Group To Identify and Publicize Priority Health Needs in Human and Animal Medicine for New AR Products (e.g., Innovative Drugs, Targeted Spectrum Antibiotics, Point-of-Care Diagnostics, Vaccines and Other Biologics, Anti-Infective Medical Devices, and Disinfectants).**

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Interagency AR product development working group | FDA has chosen to perform these cooperative activities using existing advisory committees with other agency and industry participation. | Initial AC meeting Feb 19-20, 2002. Docket available for additional comment. |
| FDA | Otitis Media Advisory Committee | Discussion of clinical study design for drugs treating acute otitis media (which may impact resistance in the pediatric population) | Meeting held on July 11, 2002. |
| FDA | FDA/PhRMA Co-Sponsored Workshop | Discussion of statistical issues in clinical trials including trials related to resistant pathogens. | Meeting held on November 9, 2002. |
| FDA | FDA/IDSA/PhRMA Co-Sponsored Public Workshop | Coordinated and hosted a public workshop that brought together top national leaders and scientists from the Infectious Disease Society of America, Pharmaceutical Research and Manufacturers of America, and U.S. academic institutions along with representatives from CDC and NIH to address current topics of interest associated with AR and antimicrobial drug development. | Meeting held on November 19-20, 2002. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of issues relating to macrolide-resistant *Streptococcus pneumoniae* (MRSP) | Meeting held on January 24, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of issues relating to AR in *Streptococcus pneumoniae* . | Meeting held on March 4, 2003. |
| FDA | Anti-Infective Drugs Advisory Committee (ADAC) | Discussion of a list of Antimicrobial Resistant Pathogens of Public Health Importance to assist stakeholders in the development of antimicrobial drugs related to resistant pathogens. | Meeting held on May 5, 2003. |
| **** TOP PRIORITY ****<br>**Action Item #80: Identify Ways (e.g., Financial and/or Other Incentives or Investments) To Promote the Development and/or Appropriate Use of Priority AR Products, such as Novel Compounds and Approaches, for Human And Veterinary Medicine for Which Market Incentives Are Inadequate.** | | | |
| FDA | New AR products | Identify and publicize priority public health needs for new AR products; identify the kinds of products we would want to see developed. | Preliminary meeting has occurred; working group is forming; future action TBD CDER advisory committee held February 2, 2002. |
| FDA | Joint efficacy workshop and advisory committee meeting | Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures of efficacy. | Completed February and March 2001. Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines held Spring 2002. |
| FDA | See Action Item #79 (Interagency AR Product Development Working Group) | See Action Item #79 (Interagency AR Product Development Working Group). | See Action Item #79 (Interagency AR Product Development Working Group). |
| FDA | Maternal immunization | Development of approaches for licensure of vaccines to prevent group B streptococcal infections. CDC, NIH, FDA meeting May 1998 regarding Maternal Immunization and NIAID, NIH Advisory meeting regarding serological assays. | Continued regulatory and research effort to remove barriers to product development under current funding. |
| FDA | Guidance document | Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals. | Working group formed; Draft document completed. |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | Noval therapeutic approaches using immunoglobulin. | Include a humanized monoclonal antibody and a respirator synctial virus human immune globulin indicated for prevention of serious lower respiratory tract diseases (caused by RSV) and sepsis. | Ongoing regulatory review and research. |
| **Action Item #81: Consider, in Consultation with Academia and Industry, Whether Government Has a Constructive Role To Play in Discovery of Drugs and Other Products Targeted To Address Areas Where Market Incentives are Limited and Unmet Needs Exist (e.g., Novel Antimicrobial Drugs Targeted To Specific Resistant Organisms).** | | | |
| FDA, CDC, NIH | Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP) | Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues. | Workshop held April 15-16, 2004. |
| FDA | New AR products | Development of Hyper-Immune Globulins | CBER role is to develop immunization protocols, assays and standards for such products. |
| **Action Item #82: Continue Ongoing Approaches that Streamline the Regulatory Process, Including Clinical Trials and Enhanced Pre-Clinical Studies (e.g., Use of Pharmacokinetics and Pharmacodynamics Data) To Help Bring AR Products (Including Drugs, Vaccines, Diagnostics and Devices) To Market as Efficiently and As Rapidly as Possible, While Still Assuring Their Safety and Efficacy.** | | | |
| FDA, CDC, NIH | Antimicrobial Drug Development Public Workshop (sponsored by FDA, IDSA and ISAP) | Workshop provided information for and gained perspective from advocacy groups, industry and others on various aspects of antimicrobial drug development, including clinical trial design issues. | Workshop held April 15-16, 2004. |
| FDA | Workshop and committee meeting on efficacy | Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures of efficacy. | Completed February and March 2001 Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines was held in Spring 2002. |
| FDA | Meningitis Vaccine Project (MVP) | MVP is a combined WHO Program for Appropriate Technology in Health (PATH) project to develop affordable meningococcal conjugate vaccines for Africa. | Scientific panel met in March 2003. Consortium of public, private, and non-profit organizations, and a philathropic organization (the Gates Foundation) will develop a vaccine that is critically needed in Africa. |
| FDA | Regulatory requirements – industry and scientific community | Clarify FDA regulatory requirements to both industry and the scientific community. | 1) Presentation on regulatory requirements for tests of use in AR initiatives to the Professional IVD Roundtable (a group representing all major professional laboratory groups) twice yearly. Discussion on obstacles and issues which might exist in technology transfer. 2) Draft guidance under development on the review and labeling of devices that contain antimicrobial agents. |
| FDA | Topical micobicides | CBER/CDER working group on Topical Microbicides. | Working group formed; Draft document completed. |
| FDA | See Action Item #80 (Maternal Immunization). | See Action Item #80 (Maternal Immunization). | See Action Item #80 (Maternal Immunization). |
| FDA | See Action Item #80 (Guidance Document). | See Action Item #80 (Guidance Document). | See Action Item #80 (Guidance Document). |
| FDA | HIV Drug Resistance Genotype Assay Guidance (See Action Item #10) | Revised guidance on HIV Drug Resistance Genotype Assays. Significantly reduces the extent of studies required for clearance. | Publication pending |

| AGENCY | PROJECT TITLE | DESCRIPTION | STATUS |
|---|---|---|---|
| FDA | See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting) | See Action Item #30 (Resistant Pathogens List Advisory Committee Meeting) | See Action Item #30 ( Resistant Pathogens List Advisory Committee Meeting) |
| **Action Item #83: In Consultation with Stakeholders and Expert Consultants, Identify Ways To Promote The Development of New and Alternative Veterinary Treatments and The Improved Use of Existing Therapies That Are Unlikely to Stimulate Resistance to Drugs in Human Medicine.** | | | |
| **Action Item #84: Streamline the Regulatory and Approval Process for Veterinary Antimicrobial Drugs and Related Products That Are Unlikely, Now or in the Future, To Result In Transfer of Antimicrobial Resistance To Humans.** | | | |